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CBT for Nightmares in OEF/OIF Veterans

PRINCIPAL INVESTIGATOR: Richard Ross, M.D., Ph.D.

CONTRACTING ORGANIZATION: Philadelphia Research and Education Foundation
Philadelphia, PA 19104

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
This study examines the efficacy of two cognitive-behavioral treatments for PTSD-related recurrent nightmares and other sleep difficulties in Veterans of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) in a randomized controlled trial. Participants were 108 OEF/OIF Veterans in outpatient treatment for PTSD at one of two study sites, the Corporal Michael J. Crescenz VAMC (CMCVAMC Philadelphia) or the VACHS, West Haven, CT. During the final year of this award, data collection was completed at the Philadelphia sites (CMCVAMC and CMCVAMC affiliated outpatient clinics). We have now analyzed outcome and ancillary data. Several poster presentations have been completed, and manuscripts and symposia are in preparation.

15. SUBJECT TERMS
Posttraumatic Stress Disorder, Nightmares, Randomized Controlled Trial, Cognitive-behavioral Treatment, OEF/OIF Veterans

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Section I: Introduction

A substantial proportion of Veterans returning from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) have significant psychological symptoms related to traumatic war zone exposure, including recurrent nightmares and other sleep disturbances. Nightmares are generally distressing and difficult to treat, often persisting despite successful resolution of other Posttraumatic Stress Disorder (PTSD) symptoms. A cognitive-behavioral treatment (CBT), Imagery Rehearsal (IR), appears to have promise for successfully treating nightmares. This study investigates the efficacy of IR in treating OEF/OIF Veterans, many of whom have mild to moderate traumatic brain injury (TBI). There are three main objectives of this study: 1) to examine the efficacy of IR, combined with psychoeducation about PTSD and nightmares and components of standard CBT for insomnia (henceforth referred to as *IR+cCBT-I*), compared to psychoeducation about PTSD and nightmares and components of CBT for insomnia (henceforth referred to as cCBT-I) alone, in reducing nightmare frequency and improving global sleep quality in OEF/OIF Veterans with PTSD; 2) to determine whether there are moderating effects of neurocognitive impairment on the efficacy of these two forms of CBT for nightmares; and 3) to explore possible neurobiological correlates of treatment-related changes in nightmare frequency and sleep quality, focusing on noradrenergic systems. One hundred and fifteen OEF/OIF Veterans enrolled in treatment for PTSD at the Corporal Michael J. Crescenz VA Medical Center (CMCVAMC), Philadelphia, PA or the VA Connecticut Health Care System (VACHS), West Haven, CT, were to be randomized to one of two individual treatments: IR + CCBT-I or CCBT-I alone. Participants were referred by their mental health treatment providers and assessed for PTSD and war zone-related nightmares. Participants completed a battery of computerized neuropsychological tests at baseline. Once randomized, participants met for six weekly individual sessions of IR + CCBT-I or CCBT-I alone. Participants complete self-report questionnaires assessing nightmares, sleep quality, PTSD, and depression at baseline, immediately after treatment, and again three and six months after treatment. Additionally, participants provided saliva samples for measurement of salivary alpha-amylase, a marker of peripheral noradrenergic activity, both before sleep onset and upon awakening, for two nights before treatment and for two nights before the first post-treatment assessment.

Section II: Progress to Date on 5 Study Tasks in Approved Statement of Work:

1. ***Obtaining approvals for the study protocol at the study locations.***
   A. Corporal Michael J. Crescenz VAMC (Philadelphia):
   - Regulatory review of the initial protocol was completed by the CMCVAMC IRB and Research and Development Committee on 6/3/2008 and the DoD HRPO on 2/13/2009.
   B. VACHS, West Haven/Yale University:
   - Regulatory review of the initial protocol was completed by the VACHS IRB and Research and Development Committee on 6/5/2008 and by the Yale University IRB on 11/12/2008. The DoD HRPO approved this protocol on 2/24/2009. The protocol for this study site was closed at Yale University on 10/13/11 and at the VACHS site on 3/7/12.

2. *Recruitment, assessment and randomization of 102 participants at the CMCVAMC site and 6 at the VACHS site (total N=108).*

    A.   <u>CMCVAMC (Philadelphia):</u>

•   Recruitment of participants was completed in June 2014, when, after a period of reduced referrals, it was determined that the effort and cost of recruitment could not be sustained and that sufficient subjects had been recruited. During the final year of recruitment, we received 140 referrals from treatment providers at the CMCVAMC site and its affiliated CBOCs.

    •   <u>CMCVAMC</u>**:** During the entire recruitment period, we received 216 referrals to this study from CMCVAMC treatment providers. Of these referrals, 78 completed the first assessment and 52 completed both assessments and were enrolled. Twenty-five participants were randomized to IR+CCBT-I and 27 to CCBT-I alone.

    •   <u>CMCVAMC CBOCs:</u> During the entire recruitment period, 238 Veterans were referred to this study by providers at the four CMCVAMC-affiliated CBOCs. Of these referrals, 15 completed the first assessment and 50 completed both assessments and were enrolled. Twenty-four participants were randomized to IR+CCBT-I and 26 to CCBT-I alone.

•   Over the course of the study, a total of 138 Veterans were assessed and 102 participants were enrolled at the Philadelphia site (CMCVAMC and CMCVAMC-affiliated CBOCs).

    B.   <u>VACHS, West Haven:</u>

•   The VACHS site received 22 referrals from treatment providers and 14 self-referrals. Assessments were scheduled with 12 potential participants, and six Veterans completed both assessments and were enrolled.

•   The VACHS site has been closed to enrollment since 4/2010.

C. <u>Overall summary statistics:</u>

•   Table 1 shows demographic characteristics of all 108 enrolled Veterans.

Table 1. Demographics and comorbid diagnoses of enrolled Veterans.

	IR+ CCBT-I (N=53)	CCBT-I (N=55)	Total (N=108)
Demographics, n (%)			
Male	47 (88.7)	46 (83.6)	93 (86.1)
Race			
Caucasian	34 (64.2)	29 (52.7)	63 (58.3)
African- American	17 (32.1)	23 (41.8)	40 (37.0)
Other	2 (3.8)	3 (5.4)	5 (4.63)
Marital status			
Married/Cohabitating	30 (57.7)	24 (44.4)	54 (50.9)

Separated/Divorced	13 (25.0)	12 (22.2)	25 (23.6)
Never married/Widowed	9 (17.3)	18 (33.3)	27 (25.5)
Education			
High school (part or completed)	20 (37.7)	17 (30.9)	37 (34.3)
College (part or completed)	33 (62.3)	38 (69.1)	71 (65.7)
Employment			
Full- or part-time	23 (43.4)	24 (43.6)	47 (43.5)
Retired/unemployed	30 (56.6)	31 (56.4)	61 (56.5)
Service Branch			
Army	34 (64.2)	34 (61.8)	68 (63.0)
Navy	2 (3.8)	6 (10.9)	8 (7.4)
Air Force	6 (11.3)	2 (3.6)	8 (7.4)
Marines	12 (22.6)	8 (14.6)	20 (18.5)
Age, mean (sd)	37.0 (9.9)	37.2 (10.1)	37.1 (9.9)
Comorbid Diagnoses			
Major Depressive Disorder	37 (69.8)	32 (58.2)	69 (63.9)
Generalized Anxiety Disorder	10 (18.9)	14 (25.4)	24 (22.2)
Alcohol Abuse	7 (13.2)	1 (1.8)	8 (7.4)
Diagnosed TBI	14 (26.4)	21 (38.2)	35 (32.4)
PTSD service connection	40 (75.5)	41 (75.9)	81 (75.5)

3. ***Administration of six sessions of the protocol treatments to participants.***

• <u>Treatment fidelity:</u> An independent doctoral level rater, external to the study and experienced with manualized treatments, use a standardized form to rate treatment fidelity. A random sample of 10% of video-recorded therapy sessions was rated to determine therapists' adherence to the treatment protocol as well as their competence in treatment delivery.

  o There were no substantial deviations from the treatment protocol, with no session rated as less than *good* on global adherence to the protocol, and 88% of rated sessions rated as *excellent*. Similarly, the interpersonal effectiveness, pacing of sessions and overall session quality were also *excellent* in 79-88% of sessions. While there was some variation across therapists, the treatment fidelity did not differ between treatment groups.

• As can be seen in the CONSORT flowchart below (Figure 1), seventy-six Veterans completed treatment, and dropout from treatment was 19% of all participants who initiated treatment, 19.6% from IR+CCBT-I, and 18.8% from CCBT-I.

Figure 1. Participant Flow throughout the Trial

Enrollment

Assessed for eligibility (n=150)

Excluded (n=42)
- Not meeting inclusion criteria (n=22)
- Declined to participate (n=16)
- Other reasons (n=4)

Randomized

Allocation

Allocated to cCBT-I (n=55)
- Received complete intervention (n=39)
- Received 1+ sessions of intervention (n=48)
- Did not receive any allocated intervention (n=7)

  Reasons: family issues (1), multiple no-shows for appointments (4), had received previous CBT-I (1), deceased (1)

Allocated to IR+cCBT-I (n=53)
- Received complete intervention (n=37)
- Received 1+ sessions of intervention (n=46)
- Did not receive any allocated intervention (n=7)

  Reasons: family issues (2), multiple no-shows for appointments (2), had started Prolonged Exposure (1), changed mind about participation (2)

Follow-up

Lost to follow-up (n= 4)
- n= 4: lost before 3-month assessment
- n=0: lost before 6-month assessment

  Reason: did not return phone calls or packets mailed- unreachable (4)

Discontinued intervention (n=9)

Lost to follow-up (n=2)
- n=1: lost before 3-month assessment
- n=1: lost before 6-month assessment

  Reason: did not return phone calls or packets mailed- unreachable (2)

Discontinued intervention (n=9)
  Reasons: moved away (1), child care (1), unstable psychiatric symptoms (1), did not think treatment was helpful (1), other life stressors (4), multiple no-

Analysis

Analyzed (n= 55)
- Excluded from analysis (n=0)

Analyzed (n= 53)
- Excluded from analysis (n=0)

4. Follow-up: reassessment for detection of treatment effects post-treatment and maintenance of benefits at 3 months and 6 months post-treatment.

- Figure 1 (CONSORT flow chart) shows that six participants dropped out between the end of treatment and 6-month follow-up.

5. Statistical analysis of the data and manuscript preparation.

- We have completed data entry and checking of the entered data. The final dataset has been assembled and is being analyzed.
- Currently, the main analyses have been completed and manuscript preparation is underway for the main RCT outcome paper (to be submitted for peer-reviewed publication in the fall of 2015). In addition to carrying out Intent-to-Treat analyses, we are analyzing potential effect modifiers in order to identify those Veterans who may be most likely to improve with one or the other of the two treatments (see section V. Conclusions).
- We have also conducted secondary analyses of the collected data. We have been presenting these at national meetings and preparing/submitting manuscripts for publication. We have one manuscript currently under review. For a list of papers and poster presentations, please see Section IV, Reportable Outcomes.
- In addition, the International Society for Traumatic Stress Studies (ISTSS) has accepted our symposium titled "Treatment of Sleep Disturbance in PTSD: Nightmare-focused and Insomnia-focused Treatments, Treatment Moderators, and the Effects of Neurocognitive Functioning" for their annual meeting in November 2015. At this meeting, we plan to present our main findings to the scientific community in three separate talks ("Treating Posttraumatic Sleep Disturbance in U.S. Veterans Who Served in Iraq and Afghanistan: Findings from a Randomized Controlled Trial"; Combat-related PTSD Nightmares: Which Veterans Benefit from Imagery Rehearsal?" and "Effects of Neuropsychological Functioning on Outcomes and Dropout in a Randomized Trial of Sleep Interventions").

Section III: Key Research Accomplishments:

- Completion of all regulatory reviews at CMCVAMC, Yale University, and VACHS, as well as the DOD HRPO.
- Hiring and training of staff at two sites and later at the CMCVAMC CBOCs.
- Participant recruitment at the CMCVAMC site and its affiliated CBOCs and at the VACHS site.
- Successful shift of recruitment from the VACHS site, which discontinued recruitment of participants for the study in April 2010, to the CMCVAMC-affiliated CBOCs.
- Successful increase in recruitment rate over the last three recruitment years such that our target enrollment (n=115) was almost achieved (final n=108) despite many challenges in recruiting from the OEF/OIF Veteran population.
- Data entry and checking completed. Statistical analyses and manuscript preparation are ongoing. We expect to submit the RCT outcome paper for publication in the fall of 2015.

Section IV: Reportable Outcomes:

Completed poster presentations:

Harb, G. C., Brownlow, J. A., and Ross, R. J. (2015). *Understanding recurrent posttraumatic nightmares: Variables contributing to nightmare symptomatology.* Poster presented at the annual meeting of the Associated Professional Sleep Societies, Seattle, WA.

Harb, G. C., Cook, J. M., Phelps, A., and Ross, R. J. (2014). *Nightmares of U.S. Iraq and Afghanistan War Veterans with PTSD: Content and characteristics.* Poster presented at the annual meeting of the International Society for Traumatic Stress Studies, Miami, FL.

Brownlow, J. A., Harb, G. C., Gehrman, P. R., Gur, R. C., and Ross, R. J. (2014). *Sleep disturbance and neurocognitive function in OEF/OIF Veterans with PTSD.* Poster presented at the annual meeting of the International Society for Traumatic Stress Studies, Miami, FL.

Harb, G. C., Waldron, E. A., Brownlow, J. A., and Ross, R. J. (2014). *Lucid dreaming and the treatment of nightmares in OEF/OIF/OND Veterans with PTSD.* Poster presented at the annual meeting of the Associated Professional Sleep Societies, Minneapolis, MN.

Harb, G. C., Cary, M., Gehrman, P., and Ross, R. (2013). *The symptoms of OEF/OIF Veterans referred to sleep and nightmare research: Are we studying a representative sample?* Poster presented at the annual meeting of the Associated Professional Sleep Societies, Baltimore, MD.

Completed paper/workshop presentations:

Harb, G. C. and Gehrman, P. (2014). *Treating the sleep disturbance in Veterans with PTSD: CBT for insomnia and imagery rehearsal.* Pre-meeting institute at the annual meeting of the International Society for Traumatic Stress Studies, Miami, FL.

Wolgast, B. and Harb, G. C. (2014). *Treatment of insomnia and nightmares: CBT-I and IRT for helping patients with sleep problems.* Workshop presentation at Coatesville VAMC, Coatesville, PA.

Cook, J., Harb, G. C., and Ross, R. J. (2013). *Imagery rehearsal for posttraumatic nightmares: Observations from two clinical trials.* Presentation at the annual meeting of the European Society for Traumatic Stress Studies (ESTSS), Bologna, Italy.

Review articles:

Brownlow, J. A., Harb G. C., and Ross, R. J. (2015). Treatment of sleep disturbances in Post-traumatic Stress Disorder: A review of the literature. *Current Psychiatry Reports, 17 (6),* 41.

Harb, G. C., Phelps, A., Forbes, D., Ross, R., Gehrman, P., and Cook, J. (2013). A critical review of the evidence base of imagery rehearsal for posttraumatic nightmares: Pointing the way for future research. *Journal of Traumatic Stress, 26,* 570-579.

Gehrman PR, Harb GC. Treatment of nightmares in the context of posttraumatic stress

disorder. J Clin Psychol. 2010;66(11):1185–1194.

Manuscripts under review:

Harb, G. C., Brownlow, J. A., and Ross, R. J. (submitted). Posttraumatic nightmares and imagery rehearsal: The role of lucid dreaming.

Section V: Conclusions:

Over the course of this project, we addressed the three specific aims we proposed to investigate in our original grant proposal.

Aim 1: *To examine the efficacy of IR, combined with psychoeducation about PTSD and nightmares and standard CBT for insomnia (IR + CCBT-I), compared to psychoeducation about PTSD and nightmares and CBT for insomnia (CCBT-I) alone, in reducing nightmare frequency or intensity and improving global sleep quality in OEF/OIF veterans with PTSD.*

- We completed a RCT with OEF/OIF Veterans with chronic, severe PTSD seeking treatment for recurrent nightmares, comparing the efficacy of two treatments: cCBT-I and IR + cCBT-I.
- Although we expected to be treating less chronic nightmares in this population compared to the cohort of Vietnam War Veterans in our previous study (Cook et al. (2010), these younger Veterans had experienced sleep and nightmare problems for several years.
  - Despite being on average 5 years post-deployment, with PTSD and sleep symptoms during this entire time, participants had been receiving pharmacotherapy and/or psychotherapy for less than one year on average.
- Both treatments succeeded in significantly reducing nightmare frequency, nightmare distress, and sleep disturbance (see Figures 2 and 3). There were clinically significant changes in both treatment groups:
  - For number of nights with nightmares per week (NFQ), both treatments showed nearly a 30% reduction at 6-month follow-up (overall average decrease from 3.6 to 2.6).
  - For nightmare distress, the NDQ dropped about 4 points from baseline, a reduction of about 14% (the overall mean NDQ score was 29.4, sd=5.79).
  - The percentages of Veterans with clinically important decreases in nightmare frequency (baseline to 6-month follow-up) in *IR+cCBT-I* (N=41) versus *cCBT-I* (N=38) were 39.0% and 42.1%, respectively (X^2(2)=0.08, p=0.78); the difference in proportions was -0.31.
  - Clinically important changes in sleep (PSQI total) were seen in 51.2% (*IR+cCBT-I*) and 44.7% (*cCBT-I*) of Veterans, respectively (X^2(2)=0.33, p=0.56;

the difference in proportions was 0.065, with a 95% confidence interval of -0.155 to 0.285).
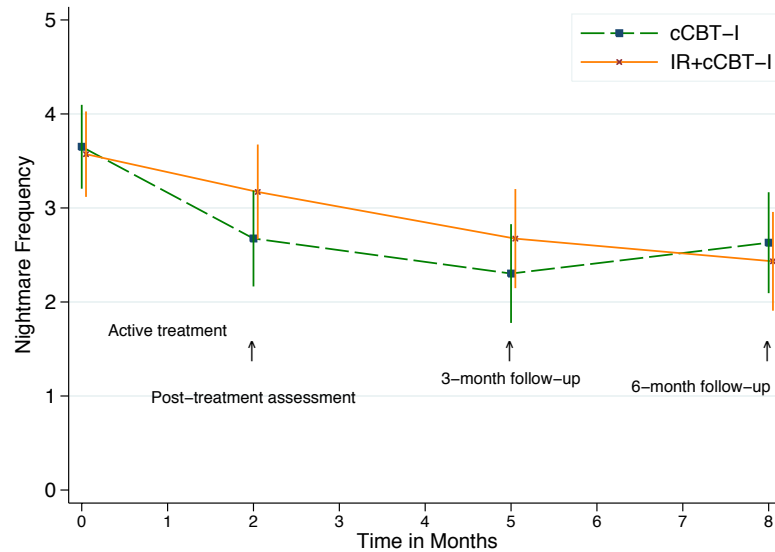

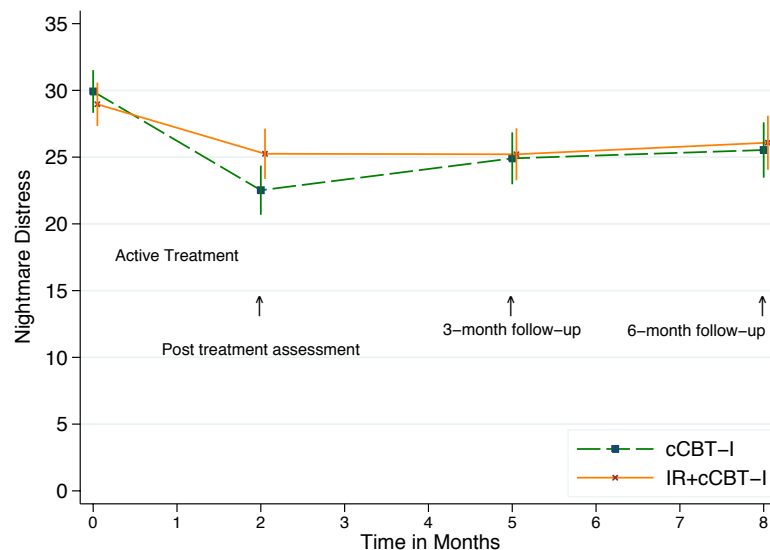Figure 2. ITT analyses reduction of nightmare frequency by group

Figure 3. ITT analyses reduction of nightmare distress by group

- ITT analyses showed that the addition of *IR* to *cCBT-I* did not, overall, result in significantly more treatment gains than *cCBT-I* alone (see Figures 2 and 3, above).
  - o IR+ cCBT-I treatment did not perform better than cCBT-I alone (Table 2, below). Means for the primary outcome measures, their confidence intervals, the estimates of the effects at each time point (i.e., the interaction term for time by treatment), and the overall omnibus test across the three (time x treatment) interaction terms support this conclusion.

o   The omnibus tests for the interactions for the weekly number of nights with nightmares ($X^2(3)=4.66$, p= 0.20), and for the nightmare distress questionnaire ($X^2(3)=7.17$, p= 0.07), did not reach conventional levels of significance. The effect sizes at 6 months post-treatment were approximately -0.06 for the weekly number of nights with nightmares (IR+ cCBT-I better than cCBT-I alone), and 0.20 for nightmare distress (cCBT-I alone better than IR+ cCBT-I).

o   The same model was run on the secondary outcomes. There were no significant omnibus effects for the weekly number of nights with nightmares ($X^2(3)=3.72$, p= 0.29), the log-transformed weekly number of nightmares ($X^2(3)=0.73$, p= 0.87), the PSQI ($X^2(3)=1.09$, p= 0.78), the PSQI-Addendum ($X^2(3)=0.49$, p= 0.92), or the PCL-M ($X^2(3)=2.46$, p= 0.48).

Table 2. Modeled Means with Model-Based Treatment Effects

	CBTi			CBTi+IR			Treatment Group Effect Interaction**		
Outcome	n*	M**	95% CI	n*	M**	95% CI	Estimate	95% CI	p
Average Nights per Week with Nightmares									
Baseline	55	3.65	3.20, 4.09	53	3.58	3.12, 4.02	--	--	--
End of treatment	38	2.67	2.16, 3.18	40	3.17	2.67, 3.68	0.57	-0.15, 1.29	.12
3 mo. post treatment	37	2.30	1.77, 2.83	37	2.67	2.14, 3.21	0.45	-0.30, 1.19	.24
6 mo. post treatment	38	2.62	2.08, 3.17	41	2.43	1.90, 2.97	-0.12	-0.87, -.63	.76
Nightmare Distress Score									
Baseline	55	29.9	28.4, 31.4	53	29.0	27.4, 30.5	--	--	--
End of treatment	38	22.5	20.7, 24.3	36	25.2	23.3, 27,2	3.63	0.94, 6.31	.008
3 mo. post treatment	37	24.9	22.9, 26.9	37	25.2	23.2, 27.2	1.25	-1.55, 4.06	.88
6 mo. post treatment	38	25.6	23.4, 27.7	41	26.2	24.1, 28.3	1.53	-1.41, 4.47	.31

* Observed n for the cell

**Modeled mean and interaction include baseline covariates of CAPS score and PSQI score

- To explore the possibility that a subgroup demonstrated a better or worse treatment response, we compared treatments in subgroups by gender, race (white vs. all other), high initial PCL-M, high nightmare severity (above median on nightmare frequency and nightmare distress), and TBI. These analyses used the same baseline covariates, PSQI and CAPS scores. For outcome variables, the NFQ and the NDQ were used (omnibus test of the 3-way interaction between treatment, time, and moderator). Two important findings emerged. First, the omnibus test for the interaction for gender approached conventional levels of statistical significance ($X^2(3)$=6.63, p=0.09). Second, those higher in initial nightmare severity were less able to benefit from treatment.
  - Women performed better with *IR+cCBT-I than cCBT-I alone,* while men did not demonstrate this effect.
    - Most successful studies of IR have treated female patients.
    - Caveat: this finding needs replication by future research due to the relatively small number of women in this study.
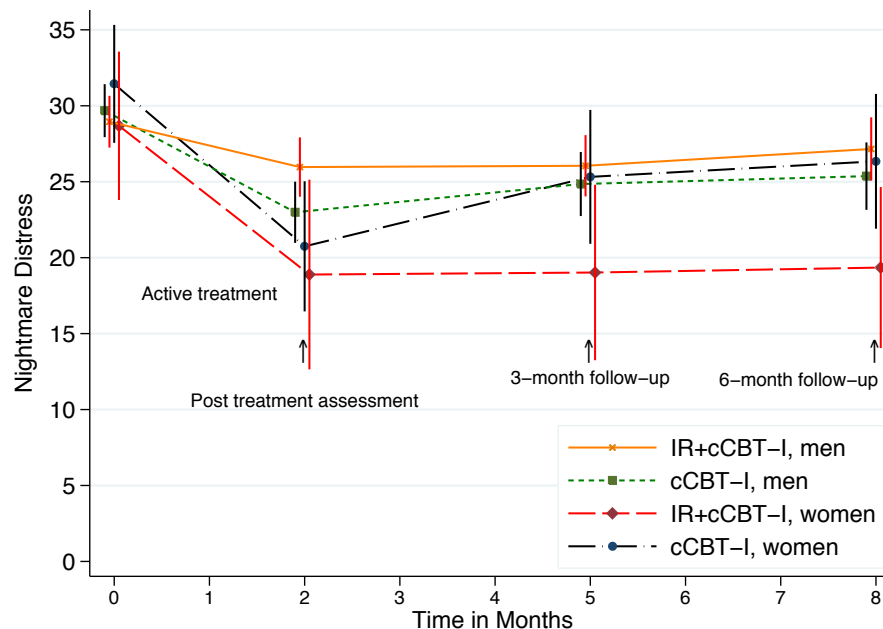

Figure 4. Treatment modification by gender and group.

  - Veterans with greater nightmare severity at baseline were not able to benefit as much from the treatments, in particular *IR+cCBT-I.*
    - Most published IR trials have treated patients with less severe, often subsyndromal, PTSD.
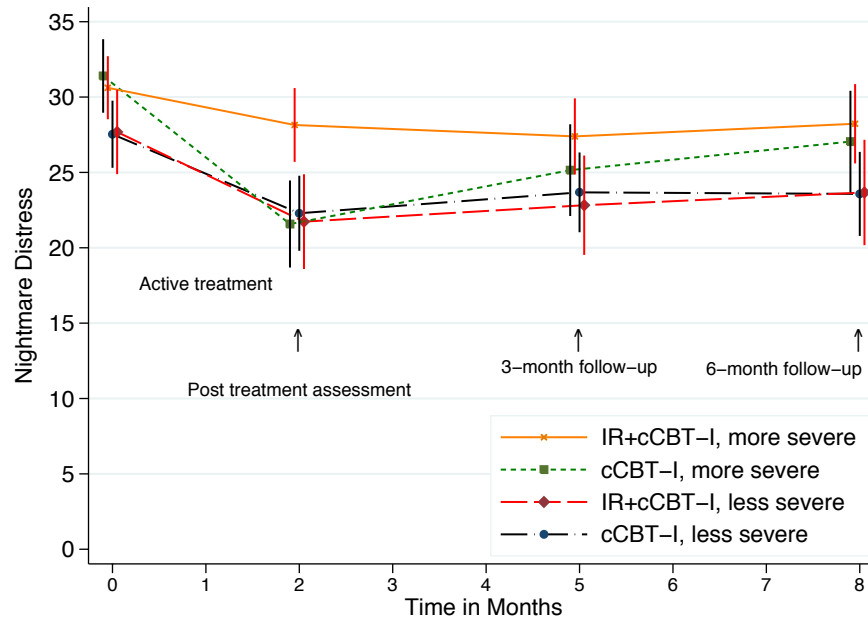
Figure 5. Treatment modification by baseline nightmare severity and group.

Aim 1. Summary & Implications:
- Although in this study, the comparison condition was not the full *CBT*-I currently most often used for insomnia treatment, it appears from these results that it may not always be necessary to add IR, for recurrent nightmares, to CBT-I for the sleep disturbance of chronic PTSD in Veterans. Our results suggest that IR could improve the performance of general sleep treatment (cCBT-I) in specific groups of Veterans, namely women and those with less severe baseline nightmare disturbance.
- Both treatments succeeded at producing clinically significant decreases in nightmare frequency and sleep disturbance.
- Results suggested that IR could improve the treatment gains in specific groups of Veterans: Women and veterans with less severe baseline nightmare disturbance
- Needs replication, but fits with prior research picture.
- As a field we can comfortably say that IR works for some people, but not everyone.
- Future directions:
  - Replication of current findings
  - Examine why may females have a differential treatment response
  - Are there other factors which distinguish those who improved with IR from those who did not?
  - Exmaine potential modifications to IR treatment protocols to increase the potency for those with more severe baseline symptoms.

Aim 2: *To examine the effects of TBI-related mild to moderate neurocognitive impairments on treatment outcomes. (please see presentation slides in appendix for details, manuscript in preparation)*

- PTSD is associated with neuropsychological deficits (e.g., verbal memory), which could affect treatment response, however neuropsychological functioning is rarely explored as influential factor in psychotherapy treatment
- Previous research:
  - Robust association with treatment compliance and outcomes in substance use treatment (Aharonovich, Nunes, & Hasin, 2003)
  - Wild and Gur (2008): treatment non-responders showed worse immediate verbal memory at baseline, and change in PTSD symptoms was associated with verbal memory
  - Nidjam et al. (2015) – pre-treatment verbal memory functioning was associated with degree of change in PTSD symptoms across two kinds of trauma-focused therapies

- A subgroup of the 108 veterans enrolled in the RCT (n=94) completed (at the baseline assessment) the Penn Computerized Neurocognitive Battery (CNB), a widely validated battery of tests assessing attention, cognitive control, learning and memory, and spatial processing and completed an assessment of TBI history. Due to the lack of treatment outcome difference, we used both therapy groups combined for these analyses.

- Results:
  - There was a main effect of TBI on nightmare distress (*p*=0.004) and nightmare nights (*p*=0.015)
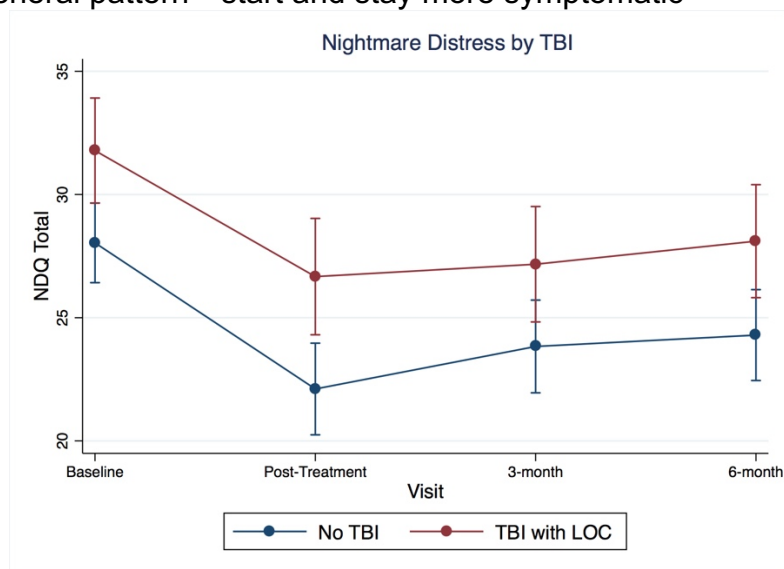 - General pattern—start and stay more symptomatic

Figure 6. Effects of TBI on treatment outcome (nightmare distress)

o   Across both treatments, individuals who showed a clinically significant improvement in sleep quality (from baseline to 6 months post-treatment) had better performance on a measure of verbal immediate memory at baseline compared to those who did not (p =.03).

o   Moreover, verbal immediate memory was significantly associated with change in nightmare distress (r=.42; p <.001) across both treatments (Figure 7), such that those Veterans with better verbal learning were more likely to experience greater reductions in nightmare distress.

- Significant verbal memory*time interaction for nightmare distress (p = .0005)
- These differences were not explained by depression or attention performance: Still significant ($p < .01$) after including depression and overall neurocognitive performance as covariates in model
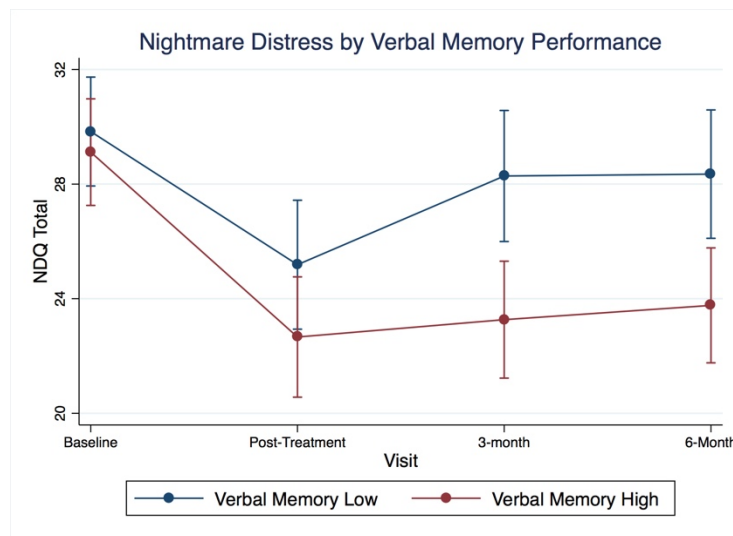

Figure 7. Change in Nightmare Distress by Verbal Memory performance

- Verbal memory*time interaction was not significant for number of nightmare nights (p = 0.40).
- Sleep quality: Significant verbal memory*time interaction for PSQI (p = 0.02); which was still significant after including overall cognitive performance as covariate in model, but including depression reduced interaction to trend (p=0.07): see Figure 8
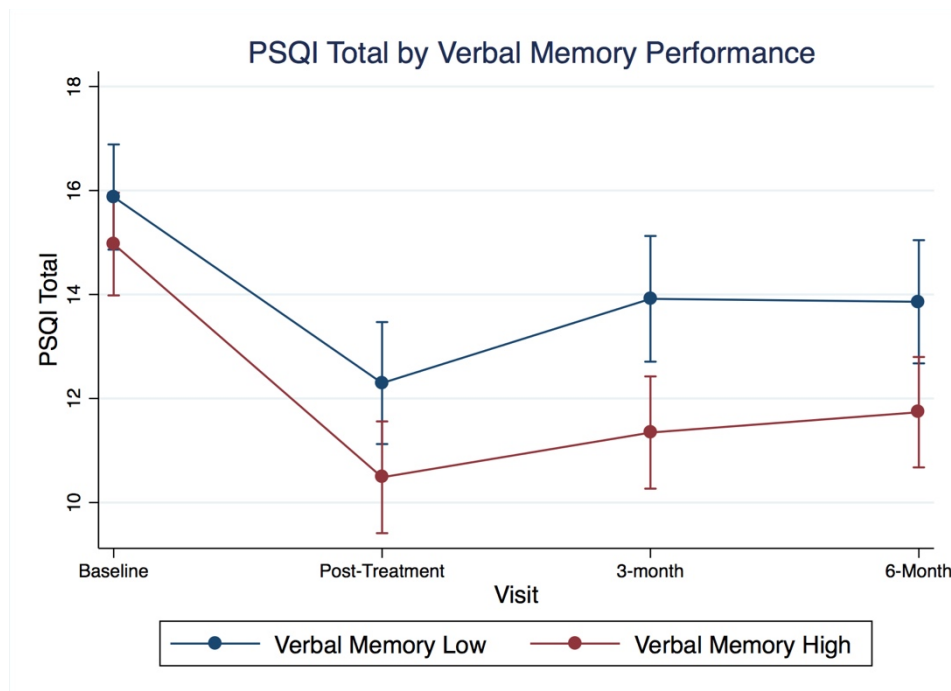
Figure 8. Change in Sleep Quality by Verbal Memory Performance

- o Dropout results:
  - ▪ Individuals with TBI not significantly more likely to drop out of treatment (OR = 0.97; *p*=.88)
  - ▪ Neither verbal memory (OR = 0.93; *p*=.73) nor working memory performance (OR = 0.64; *p*=.06) associated with treatment dropout
- Aim 2: Summary & Conclusions:
  - o Verbal memory performance moderated treatment outcomes across two types of short-term psychotherapy sleep interventions
    - ▪ Individuals with lower performance less likely to respond to treatment
  - o In combination with prior findings, results suggest that verbal memory may be important factor to consider to optimize psychotherapy treatment outcomes in PTSD; also, specifically of verbal memory.
  - o TBI may be important to consider in terms of symptom severity but did not moderate treatment response.
  - o Neither TBI nor cognitive performance was associated with treatment dropout.

  - o In summary, results indicate the importance of considering neuropsychological functioning in treatment implementation and outcome.

Aim 3: *To explore the role of noradrenergic (NA) hyperactivity in the nightmares and insomnia of PTSD, and any changes in NA activity associated with treatment outcomes.*

- Initial analyses did not support our hypothesis that improvements in the nightmare disturbance and insomnia would show evidence of being mediated by decreased NA activity.
- We expected both treatment groups to demonstrate a reduction in norepinephrine (NE) and its putative marker salivary alpha-amylase, with the IR+cCBT-Igroup displaying larger decreases.
- We will continue to examine other aspects of the possible significance of this interesting biomarker of NA hyperactivity.

Additional investigations beyond aims 1-3 (manuscripts in preparation):

Lucid Dreaming (manuscript submitted for publication):

Lucid dreams represent a distinctive state of dreaming that is characterized by awareness of dreaming and, at times, ability to control dream events and/or purposefully awaken from the dream. Lucid dreaming constructs and the role of lucid dreaming as a possible mechanism of action of imagery rehearsal therapy were investigated in Veterans with posttraumatic stress disorder and recurrent nightmares. We examined thirty-three treatment-seeking combat Veterans participating in our large clinical trial of one of two treatments*: cCBT-I* or *IR+cCBT-I*. Before treatment, Veterans demonstrated a lucid dreaming profile characterized by high dream awareness and low dream content control. Lucid dreaming constructs were not associated with baseline posttraumatic or sleep symptomatology. After *Imagery Rehearsal + cCBT-I* treatment, lucid control of dream content increased more than after *cCBT-I* treatment (*ES*=1.01; see Figure 9). An increase in dream content control was related to a reduction in nightmare distress. In summary, an increase in a component of lucid dreaming, namely content control in ongoing dreams, may be one mechanism of change in imagery rehearsal treatment. Imagery rehearsal for recurrent posttraumatic nightmares may be enhanced by incorporating lucid dreaming training.
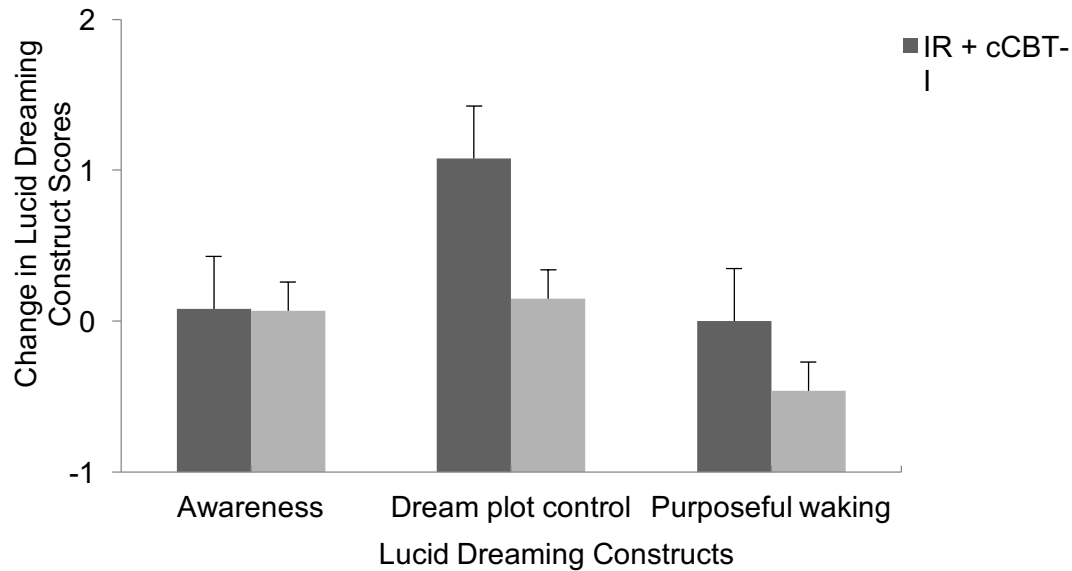
Figure 9. Lucid Dreaming Baseline to Post-treatment Change Scores as a Function of Treatment Group

Qualitative Analyses of IR treatment variables: The beginnings of these analyses were presented at the annual meeting of ISTSS (please see appendix for presentation slides) and a manuscript is in preparation. Three sources of data were examined: nightmare and revised dream scripts, therapists' narratives, participants' 6-month follow-up self report.

A.   In order to determine who most benefited from IR, we looked in-depth at data from 29-33 participants who <u>completed</u> IR in our RCT. Two doctoral level psychologists coded the content and characteristics of the target nightmare scripts and the changed dream scripts.

- Results:
  - Veterans' nightmares were gruesome.
  - Guilt nightmares may be more difficult to treat.
  - The changes made in the dream scripts were generally not related to outcome.
  - Clinical implication: we shouldn't suggest one type of change. The changes needs to be "individualized."
  - We may want to encourage our patients to change the setting so that they don't stay in deployment or war-zone scene.

B.   We coded veteran engagement, motivation, and barriers to treatment in the therapists' qualitative narratives they completed at end of treatment.

- Results:
  - Level of veterans' engagement was positively related to whether or not patients had significant changes in their nightmare symptoms ($r= .40$, p=.03)
  - Women showed higher level of engagement
  - It seems particularly important that the patient is engaged in IR:

- This fits with the retrieval competition hypothesis: If the new imagery is not rehearsed, it is not readily accessible to dreamer and cannot compete with the nightmare images which are well-rehearsed.

C. Examined veterans' six-month post-treatment qualitative report on most helpful aspects of therapy.
  - 92.6% of Veterans told us that they continued to practice skills:
  - On average, they practiced several times a week
  - 33.3% practiced CBT-I skills nightly
  - 11.1 % practiced IR skills nightly
  - Level of engagement during treatment was related to continued CBT-I practice (r=.31) and continued IR (r=.24), albeit not statistically significantly
  - Those who were rated as having made significant changes in treatment were likely to report applying IR to additional nightmares since treatment (r=.41, p<.05)

Overall implications:
- Individualized Treatment:
  - Both ratings of dream scripts and therapist narratives showed that a variety of changes in nightmares can lead to beneficial outcomes.
- Motivation & Engagement in Treatment is Very Important: predicts change during therapy and continued practice
  - Strategies for motivation enhancement may help
  - Likely important to specifically address treatment rationale and barriers to engagement

Conclusion:

In conclusion, this project resulted in important outcomes to further advance the field of nightmare-focused treatments. Our findings are consistent with other recent findings and discussions about the role of gender in treatment response and lay the groundwork for an in depth investigation of predictors of treatment response, with the ultimate objective of developing clinical guidelines for choosing certain treatments for particular individuals. With DoD funding, our group of investigators has gained invaluable experience in administering IR to Veterans, and has shared our experience and findings with other clinicians in several workshops and presentations.

Funding for this project also has allowed us to examine important novel aspects of posttraumatic sleep phenomenology and nightmares (i.e., lucid dreaming and neuropsychological functioning) that will likely prove important for a better understanding of these very significant clinical problems and their amelioration with novel treatments.

List of personnel who received research funding from this project:

- Gerlinde Harb
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- Russell Localio
- Elizabeth Waldron
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- Gabrielle Sarlo
- Daniel Libby
- Sara Michelson
- Rachel Torello
- Ilan Harpaz-Rotem

Appendix: Poster/presentation abstracts and papers

1. Harb, G. C., Brownlow, J. A. & Ross, R. J. (2015). *Understanding recurrent posttraumatic nightmares: Variables contributing to nightmare symptomatology.* Poster presented at the annual meeting of the Associated Professional Sleep Societies, Seattle, WA.

Understanding Recurrent Posttraumatic Nightmares: Variables Contributing to Nightmare Symptomatology

Gerlinde C. Harb[1], Janeese Brownlow[1,2], Richard J. Ross[1,2]
1. Philadelphia VA Medical Center
2. University of Pennsylvania, Philadelphia, USA

Introduction:
Although posttraumatic sleep disturbance is a prominent feature of PTSD, its phenomenology and factors associated with increased risk for nightmare disturbance are not well understood. Prior research has identified higher PTSD severity, vigilance and worry, lower unit support and reduced cognitive distraction as predictive of more severe general sleep disturbance. This study examined factors which may characterize those veterans more prone to persistent nightmares.

Methods:
Participants were 108 male and female (14%) OEF/OIF/OND veterans with PTSD, insomnia and recurrent nightmares in a RCT of sleep and nightmare treatments. We assessed baseline independent variables (clinician-rated PTSD severity (adjusted for nightmare symptoms), depression, deployment-related experiences, and demographics to predict nightmare symptoms: frequency (NFQ), distress (NDQ) and daytime effects of nightmares (NES).

Results:
After adjusting for demographics, PTSD severity (B = .07, SE = .03, p = .03) and combat exposure (B = .26, SE= .11, p = .02) were significant predictors of nightmare frequency; deployment perceived threat (B= .14, SE = .06, p = .02) significantly predicted nightmare distress; and depressive symptoms (B = .18, SE = .08, p = .04) significantly predicted nightmare effects. Demographics, psychological (PTSD severity, depression) and deployment factors accounted for 24% of the variance in nightmare frequency, 28.8% of the variance in nightmare distress, and 21.4% of the variance in nightmare effects.

Conclusions:
Different aspects of the nightmare disturbance of OEF/OIF/OND veterans are associated with different predictors. While PTSD and combat exposure is important in determining the frequency of recurrent nightmares, the distress associated with those nightmares (the variable more related to treatment-seeking) is affected by the perceived threat level during deployment. Results reinforce the importance of distinguishing between nightmare frequency and nightmare distress in assessing posttraumatic nightmares clinically and in future research.

2. Harb, G. C., Cook, J. M., Phelps, A. & Ross, R. J. (2014). Nightmares of U.S. Iraq and Afghanistan War Veterans with PTSD: Content and Characteristics. Poster presented at the annual meeting of the International Society for Traumatic Stress Studies, Miami, FL.

Title: **Nightmares of U.S. Iraq and Afghanistan War Veterans with PTSD: Content and Characteristics**

Authors: Gerlinde C. Harb, PhD[1], Joan M. Cook, PhD[2], Andrea Phelps, PhD[3], Richard J. Ross, MD, PhD[1,4]
Institutions: [1]Philadelphia Veterans Affairs Medical Center, Philadelphia, PA; [2]Department of Psychiatry, Yale University, New Haven, CT; [3]Australian Centre for Posttraumatic Mental Health, Department of Psychiatry, University of Melbourne, Melbourne, Australia;[4] Department of Psychiatry, University of Pennsylvania, Philadelphia, PA

OEF/OIF Veterans often suffer from posttraumatic sleep problems including nightmares. This study examined the nature of traumatic nightmares and their relationship to other psychiatric symptoms. The 25 Veterans with PTSD enrolled in a controlled trial and randomized to Imagery Rehearsal therapy included 12% women, had an average age of 35.7 (SD=10.5), and severe PTSD (mean CAPS=84.6, SD=12.6) and sleep disturbance (mean PSQI=14.8, SD=2.5) with an average of 5.8 (SD=4.9) nightmares per week. Veterans selected a recurrent combat-related nightmare and wrote it out in as much detail as possible. Two independent raters coded nightmare features, content, and themes. Most nightmares were set on deployment (84%) and were replays of traumatic events (52%) or a mixture of replay and symbolic dreams (44%). Life threat was present in the majority of nightmares (84%) and an average threat level of 3.0 (scale 0-4) showed the dreamer was usually in danger. Perpetrator content was absent from all 25 nightmares, and only one nightmare included an active act of inflicting severe injury to another person. However, most (68%) nightmares included scenes of death or severe injury, predominantly to fellow American soldiers (83%). The degree of life threat in the nightmare was not significantly related to nightmare distress. Additional results and clinical and research implications will be discussed.

3.   Brownlow, J. A., Harb, G. C., Gehrman, P. R., Gur, R. C., Ross, R. J. (2014). *Sleep disturbance and neurocognitive function in OEF/OIF veterans with PTSD.* Poster presented at the annual meeting of the International Society for Traumatic Stress Studies, Miami, FL.

Title: **Sleep Disturbance and Neurocognitive Function in OEF/OIF Veterans with PTSD**

Authors: Janeese A. Brownlow, PhD[1], Gerlinde C. Harb, PhD[2], Philip R. Gehrman, PhD[2,1], Richard J. Ross, MD, PhD[2,1]
Institutions: [1]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, USA; [2]Philadelphia Veterans Affairs Medical Center, Philadelphia, PA, USA

Insomnia and recurrent nightmares are prominent symptoms of posttraumatic stress disorder (PTSD) in Veterans. Both sleep disturbance and PTSD are associated with neurocognitive impairments in concentration, memory, and attention. This study in Iraq and Afghanistan (OEF/OIF) Veterans with PTSD examined the extent to which sleep disturbance and PTSD

severity are associated with impaired neurocognitive function. Seventy-five OEF/OIF Veterans (14.9% female; mean age 37.34, *SD* = 9.84) were recruited from the Philadelphia VA. The participants' symptomatology was assessed using the CAPS, the Nightmare Frequency Questionnaire, the Nightmare Distress Questionnaire, and the Pittsburgh Sleep Quality Index (PSQI). A Computerized Neurocognitive Battery was utilized to assess neurocognitive functions including memory, attention, executive function, and sensorimotor speed. PSQI and CAPS scores were not associated with neurocognitive measures. Nightmare frequency was significantly associated with poorer performance on tests of sustained attention (*r* = -.29, *p* = .014) and executive function (*r* = -.26, *p* = .030), and nightmare distress was associated with poorer performance on a test of spatial memory (*r* = -.27, *p* = .019). While PTSD severity and overall sleep quality were unrelated to neurocognitive performance, nightmare frequency and distress were associated with functional outcomes.

4.   Harb, G. C., Waldron, E. A., Brownlow, J. A. & Ross, R. J. (2014). *Lucid dreaming and the treatment of nightmares in OEF/OIF/OND veterans with PTSD.* Poster presented at the annual meeting of the Associated Professional Sleep Societies, Minneapolis, MN.

Title: Lucid dreaming and the treatment of nightmares in OEF/OIF/OND Veterans with PTSD.

Authors: Gerlinde C. Harb[1], Elizabeth A. Waldron[1,2], and Richard J. Ross[1,3]

Introduction: Frequent, distressing nightmares are prevalent among Veterans with PTSD. Cognitive-behavioral treatments for posttraumatic nightmares, under the umbrella title *Imagery Rehearsal (IR),* have received increasing attention. A core objective of IR is increasing feelings of mastery over negative dream content. *Lucid dreaming* is the reflective awareness and metacognitive monitoring of an ongoing dream; it has not been studied in posttraumatic nightmares. We hypothesized that lucid dreaming would be related to baseline sleep and other posttraumatic symptomatology, and that lucid dreaming experiences would increase with IR.

Methods: Fourteen OEF/OIF/OND Veterans with PTSD and recurrent nightmares participating in an ongoing RCT comparing CBT-insomnia (CBT-I) alone and CBT-I+IR have to date completed the Lucid Dreaming subscale of the Iowa Sleep Experiences Scale; this assesses 3 aspects of lucid dreaming: dream awareness, control of dream content, and purposeful waking. Other measures included the Nightmare Frequency Questionnaire (NFQ), the Nightmare Distress Questionnaire (NDQ), the Pittsburgh Sleep Quality Inventory (PSQI), and the PTSD Checklist-Military (PCL-M). Pre- and post-treatment data were obtained.

Results: At pre-treatment, lucid dreaming was uncommon (median for awareness and waking = several times a year; for control of dream content = never) and was not significantly related to fewer nightmares, less nightmare-related distress, severity of PTSD, or sleep symptomatology. Only the CBT-I+IR group significantly increased their subjective control of nightmare content (*t(7)*=2.4, *p*<.05). Furthermore, CBT-I+IR compared to CBT-I alone resulted in greater changes in control of nightmare content and purposeful waking (*t(12)*=2.6 and *t(12)*=2.4,* respectively, *p*<.05). Although not significant likely due to the small *n*, change in Veterans' ability to control nightmare content was also correlated with reduction in post-treatment nightmare frequency (*r*=.62) in the CBT-I+IR group.

Conclusions: Lucidity of dreams appears to be an important factor in the treatment by CBT-I+IR of recurrent nightmares in PTSD. Implications for research on nightmare phenomenology and treatment are discussed.

5.   Harb, G. C., Cary, M., Gehrman, P., Ross, R. (2013). *The Symptoms of OEF/OIF veterans referred to sleep and nightmare research: Are we studying a representative sample?* Poster presented at the annual meeting of the Associated Professional Sleep Societies, Baltimore, MD.

The symptoms of OEF/OIF Veterans referred to sleep and nightmare research: Are we studying a representative sample?

Gerlinde C. Harb[1], Mark Cary[2], Richard J. Ross[1,2]

Introduction: Many investigators and clinicians have noted the difficulty in engaging and retaining Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) Veterans with PTSD in treatment. This problem extends to involving these Veterans in treatment outcome research.

Methods: In our ongoing randomized clinical trial comparing two cognitive-behavioral interventions for PTSD-related insomnia and nightmares, a substantial number of OIF/OEF Veterans have chosen not to participate after agreeing to be referred by their mental health provider. We compared several characteristics (PTSD symptoms and sleep/nightmare problems) of those who went on to participate and those who did not.

Results: Of 180 referrals, 94 Veterans were assessed for inclusion in the study. Of these, 13 did not meet inclusion criteria (including PTSD diagnosis, bi-weekly nightmares, no excessive alcohol use, and no severe TBI) and 14 dropped out before enrollment (most due to presumed loss of interest). Sixty-three Veterans (13% females) were enrolled and randomized, and nine others dropped out after randomization but before engaging in any intervention. Preliminary results suggest that the two groups were not significantly different in terms of PTSD severity (CAPS total: $t=0.61$, *ns*), PTSD symptom clusters on the CAPS (re-experiencing: $t=1.23$, *ns;* avoidance: $t=0.26$, *ns*; hyperarousal: $t=0.75$, *ns*) and sleep symptomatology (nightmare and insomnia items on the CAPS, $t=.70$, $t=1.98$, *ns*, respectively).

Conclusion: Participants in treatment outcome studies are a group of patients who express interest in a particular treatment and are selected by their providers and the study inclusion criteria. Nevertheless, we see many patients discontinue their participation after some or all of the assessment is complete, similar to the failure to follow-through seen in OEF/OIF clinical populations. This investigation suggests that the veterans we treat as part of our clinical trial are similar to the larger population of referred OEF/OIF veterans. We speculate that drop out may be more determined by life situations than PTSD symptomatology.

6. Cook, J., Harb, G. C. & Ross, R. (2013). *Imagery Rehearsal for posttraumatic nightmares: Observations from two clinical trials.* Presentation at the annual meeting of the European Society for Traumatic Stress Studies (ESTSS), Bologna, Italy.

Imagery Rehearsal for Posttraumatic Nightmares: Observations from Two Clinical Trials
Authors: Cook, J., Harb, G & Ross, R. (2013)

Imagery Rehearsal (IR), a cognitive-behavioral therapy for the treatment of posttraumatic nightmares, involves selecting a target nightmare, changing the storyline, and rehearsing the new dream image. This presentation will review outcome and dropout findings from a randomized controlled trial (RCT) of IR in 124 U.S. Vietnam Veterans with PTSD and recurrent nightmares. Intent-to-treat analyses showed that, with nightmare frequency and sleep quality as outcome measures, Veterans who received six sessions of manualized IR delivered in group format had not improved significantly more than Veterans in the comparison condition.. IR did not produce substantive improvement in these older U.S. Veterans with chronic, severe PTSD. Dropout was higher in the IR condition than in the comparison psychotherapy condition. This presentation will also highlight observations from an ongoing RCT with more recent American military returnees from the wars in Iraq and Afghanistan. Participation in this trial is high and tentative impressions are promising.

7. ISTSS (Nov. 2015): PDF Slides from the Symposium appended to report

Symposium: Treatment of Sleep Disturbance in PTSD: Nightmare-focused and Insomnia-focused Treatments, Treatment Moderators, and the Effects of Neurocognitive Functioning.

Recent years have seen an increased focus on the sleep disturbance in PTSD as a primary focus of treatment. This symposium reports on outcome data from a large randomized clinical trial comparing two active cognitive-behavioral treatments of posttraumatic sleep disturbance in U.S, Veterans who served in Afghanistan and Iraq. Four presentations will focus on important facets of the treatment of the sleep problems in this population. First, the differential response to two sleep-focused cognitive-behavioral interventions will be described. Second, we will discuss the content of Veterans' nightmares and qualitative aspects of changes with Imagery Rehearsal therapy. Third, we will report on the effects of veterans' neurocognitive functioning on treatment outcome and dropout. Finally, the discussant will place the findings reported in these presentations into the larger context of the state of the science of sleep research in PTSD.

Presentation 1:
Treating Posttraumatic Sleep Disturbance in U.S. Veterans Who Served in Iraq and Afghanistan: Findings from a Randomized Controlled Trial

Gerlinde C. Harb, Joan Cook, Andrea Phelps, David Forbes, Philip Gehrman, Ilan Harpaz-Rotem, Russell Localio, Mark Cary & Richard Ross

Imagery Rehearsal (IR) has received increasing attention as a treatment for posttraumatic nightmares. This randomized controlled trial (RCT) examined whether IR added to components of CBT for insomnia (cCBT-I) provides additional benefit in treating PTSD sleep problems compared to cCBT-I alone. The primary outcomes of the RCT in 108 U.S. veterans with severe PTSD (mean CAPS= 85.5) and sleep disturbance (mean weekly nightmares= 5.4) will be presented. ITT analyses using longitudinal mixed effects models found that nightmare frequency and distress decreased from baseline to follow-up, with no significant difference between the treatments. The percentages of veterans with clinically significant decreases in nightmare frequency (baseline to 6 months post) in *IR+cCBT-I* (N=41) versus *cCBT-I* (N=38) were 39.0% and 42.1%, respectively ($X^2(2)=0.08$, p=0.78)). Clinically significant changes in sleep were seen in 51.2% and 44.7% of veterans, respectively ($X^2(2)=0.33$, p=0.56). Further, both groups reported reductions in general sleep disturbance (p < .001). The presentation will also discuss findings from subgroup analyses of the characteristics of those veterans who improved with each of the two treatments to elucidate important treatment- moderating factors. These results will be interpreted in the context of the current evidence base for nightmare- and insomnia-focused treatments.

Presentation 2:
Combat-related PTSD nightmares: Which Veterans Benefit from Imagery Rehearsal?

Joan Cook, Gerlinde Harb, Andrea Phelps & Richard Ross
Imagery Rehearsal (IR) is an emerging treatment for combat-related PTSD nightmares but much remains to be learned about which veterans are most likely to benefit. This study investigated the response of 33 U.S. veterans in the IR group of an RCT. General factors including treatment engagement and adherence, as well as specific factors pertaining to the nightmares (e.g. nature of the targeted nightmares and the rescripted dream) were assessed. New dream scripts were more often realistic (66%) rather than fantastic in nature. Most (55%) began in a military context and then changed to a different setting. The most common nightmare themes were *safety* (43%), *self-efficacy* (27%) and *enjoyment-of-life* (24%). In terms of treatment outcome, nightmares themes of *guilt* and *danger* were related to significantly less improvement in nightmare distress (*r*=.37; .35) and nightmare frequency (*r*=.66; .42). The types of changes (setting, sensory detail, themes) made in the new scripts were generally unrelated to outcome. Ratings of treatment engagement (motivation/ambivalence, barriers, expectancy) as well as treatment adherence and imagery practice, and the effects of these variables on treatment outcome will also be presented. Finally, we will address the nature of changes observed within IR through a qualitative analysis of therapists' reports integrated with sleep and nightmare diary data.

Presentation 3:
Effects of Neuropsychological Functioning on Outcomes and Dropout in a Randomized Trial of Sleep Interventions

Scott James, [1], Harb Gerlinde, PhD[2], Brownlow Janeese, PhD[3], Gur Ruben, PhD[3]
Abstract Body: Posttraumatic stress disorder (PTSD) is associated with neuropsychological

deficits (e.g., verbal memory), which could affect treatment response. As part of a trial of two cognitive-behavioral treatments for PTSD-related sleep problems, 94 U.S. Veterans completed (at study entry) the Penn Computerized Neurocognitive Battery (CNB), a widely validated battery of tests assessing attention, cognitive control, learning and memory, and spatial processing. Across both treatments, individuals who showed clinically significant improvements in sleep quality (from baseline to 6 months post) had better performance on a measure of verbal immediate memory at baseline compared to those who did not show significant improvements (p =.03). Moreover, verbal immediate memory was significantly associated with change in nightmare distress (r=.42; p <.001) across both treatments, such that those with better verbal learning were more likely to experience greater reductions in nightmare distress. These differences were not explained by depression or attention performance. The presentation will also discuss effects of traumatic brain injuries on treatment outcomes and the effects of neuropsychological functioning on treatment adherence and dropout. Results indicate the utility of considering neuropsychological functioning in treatment implementation and outcomes.

Manuscripts under review (pdf document appended):

Harb, G. C., Brownlow, J. A. & Ross, R. J. (submitted). Posttraumatic nightmares and imagery rehearsal: The role of lucid dreaming.

Review articles:

Brownlow, J. A., Harb G. C. & Ross, R. J. (2015). Treatment of sleep disturbances in Post-Traumatic Stress Disorder: A review of the literature. *Current Psychiatry Reports, 17 (6),* 41.

Harb, G. C., Phelps, A., Forbes, D., Ross, R., Gehrman, P., & Cook, J. (2013). A critical review of the evidence base of Imagery Rehearsal for posttraumatic nightmares: Pointing the way for future research. *Journal of Traumatic Stress, 26,* 570-579.

Gehrman, P. R., Harb G. C. (2010). Treatment of nightmares in the context of posttraumatic stress disorder. *Journal of Clinical Psychology, 66(11):*1185–1194.

Treatment of Sleep Disturbances in Post-Traumatic Stress Disorder: A Review of the Literature

Janeese A. Brownlow[1,2,3] · Gerlinde C. Harb[2] · Richard J. Ross[1,2]

Abstract Sleep disturbances are among the most commonly endorsed symptoms of post-traumatic stress disorder (PTSD). Treatment modalities that are effective for the waking symptoms of PTSD may have limited efficacy for post-traumatic sleep problems. The aim of this review is to summarize the evidence for empirically supported and/or utilized psychotherapeutic and pharmacological treatments for post-traumatic nightmares and insomnia. While there are few controlled studies of the applicability of general sleep-focused interventions to the management of the sleep disturbances in PTSD, evidence is growing to support several psychotherapeutic and pharmacological treatments. Future investigations should include trials that combine treatments focused on sleep with treatments effective in managing the waking symptoms of PTSD.

Keywords Psychotherapy · Pharmacotherapy · Sleep disturbance · Insomnia · Nightmares · Post-traumatic stress disorder

✉ Janeese A. Brownlow
  brownlow@mail.med.upenn.edu

1   Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

2   Philadelphia VA Medical Center, Philadelphia, PA, USA

3   Center for Sleep and Circadian Neurobiology, Behavioral Sleep Medicine Program, University of Pennsylvania, Philadelphia, PA, USA

Introduction

Sleep disturbance is a core feature of post-traumatic stress disorder (PTSD) and has been called its hallmark symptom [1]. Although insomnia and recurrent nightmares are included in the diagnostic criteria for PTSD, other sleep disturbances, including obstructive sleep apnea (OSA) [2], periodic limb movement disorder (PLMD) [3, 4], and rapid eye movement sleep behavior disorder (RBD) [5], also have been linked to PTSD. Mood disorders, anxiety disorders, and substance use disorders are often comorbid with PTSD [6] and may also affect the clinical course of this disorder, including the associated sleep disturbances.

Sleep mechanisms have been linked to the development and maintenance of PTSD [7]. Insomnia and recurrent nightmares are two of the most common and distressing symptoms of the disorder [8–10], and they generally exacerbate the waking symptoms of PTSD [11, 12]. Despite the significance and high prevalence of these sleep disturbances, studies of the first-line treatments of PTSD, both psychotherapeutic and pharmacological, rarely examine the effectiveness of these therapeutic modalities for PTSD-related sleep symptoms. This is especially problematic given the evidence for clinically significant residual sleep problems during and following PTSD treatment [13•, 14, 15••]. Finally, persistent symptoms of insomnia and recurrent nightmares have the potential to compromise treatment responses to empirically supported PTSD interventions.

The primary aim of this review is to summarize psychotherapeutic and pharmacological interventions for insomnia and recurrent nightmares in PTSD. We first provide a brief background on the phenomenology of the insomnia and recurrent nightmares. It should be noted that we do not use the terms insomnia and nightmares to refer to formal diagnoses included in the Diagnostic and Statistical Manual of Mental

Disorders (5th ed.; DSM-5) [16] or the International Classification of Sleep Disorders (ICSD) [17]. Rather, "insomnia" refers to the difficulty sleeping that is a Criterion E hyperarousal symptom of PTSD, and "nightmares" refer to the recurrent distressing trauma-related dreams that are a Criterion B reexperiencing symptom of the disorder. We proceed to discuss sleep disorders and mental disorders that may be comorbid with PTSD, and the implications for treating sleep disturbances in PTSD. Finally, we review the different forms of psychotherapy and pharmacotherapy that have shown utility in treating insomnia and recurrent nightmares in PTSD.

Insomnia and PTSD

Approximately 70 % of individuals with PTSD report difficulty in initiating and maintaining sleep [8]. Insomnia in individuals with PTSD has been linked to increased psychiatric comorbidity, including alcohol use and poor health status [18]. Also, recent studies demonstrate that insomnia symptoms predating the trauma may be an important predictor of, or independent risk factor for, the development of PTSD [19, 20•, 21•]. Gehrman and colleagues [20•] found that pre-deployment insomnia symptoms in members of the military significantly increased the risk of developing PTSD, depression, and anxiety disorders following deployment. Similarly, Wright and colleagues [21•] found that insomnia symptoms at 4 months post-deployment were a significant predictor of PTSD symptoms as well as depression at 12 months post-deployment. Taken together, these studies highlight the importance of assessing and treating insomnia in both individuals at high risk for developing PTSD and in individuals with established PTSD.

Recurrent Nightmares and PTSD

Recurrent trauma-related nightmares are another highly prevalent and distressing feature of PTSD. Research suggests two types of post-traumatic nightmares, symbolic and replicative [22]. Symbolic nightmares contain normal dream content, with distortions, irrational structures, and eidetic images, with some aspect of the trauma being represented symbolically. On the other hand, replicative nightmares, which have been viewed as highly specific to PTSD, seem to replicate part or all of the traumatic event(s); their content is more logical and lacking in the distortions characteristic of normal dreaming [22, 23]. Estimates of the prevalence of a nightmare disturbance in PTSD vary due to differences in methodology, in particular, the criteria and tools used to define and assess nightmares across studies [24]. By self-report, 52 to 96 % of individuals with PTSD endorsed experiencing frequent nightmares [10, 25]. Similar to insomnia, persistent nightmares in

the wake of a traumatic event may predict the subsequent development of PTSD and other psychiatric disorders [25–27]. For example, post-traumatic nightmares within 1 month of experiencing a traumatic event predicted greater PTSD symptom severity 6 weeks and 1 year following the event [28, 29].

Recurrent nightmares have been associated with poor overall sleep quality [30, 31], depression, and heightened risk of suicide [32–34]. Sjostrom and colleagues [34] found that nightmare sufferers had a five-fold increase in suicidality even after controlling for psychiatric diagnosis. There has been increased recognition that persistent nightmares, particularly those seen in PTSD, often require targeted treatment interventions [35].

Obstructive Sleep Apnea and PTSD

OSA is characterized by sleep-related decreases (hypopneas) or pauses (apneas) in respiration [17]. OSA estimates in the general population range from 3 to 7 % in men and 2 to 5 % in women [36]. OSA is commonly comorbid with PTSD, as well as other psychiatric [2] and medical disorders [37]. Sharafkhaneh and colleagues [2] found that individuals with OSA compared to a group without this condition had a higher prevalence of PTSD, depression, anxiety, psychosis, and dementia, with the highest comorbidity rates for depression (21.8 %), PTSD (11.9 %), and other anxiety disorders (16.7 %). OSA is particularly prevalent in PTSD and other trauma-exposed populations, with estimates ranging from 40 to 90 % [38–41]. Yesavage and colleagues [42] recently reported that 69 % of Veterans with PTSD had an apnea-hypopnea index (AHI) >10, indicative of at least mild OSA. The causes, consequences, and possible mechanisms of the reported association between OSA and PTSD require further investigation [2, 43], as do the implications for treatment of these two disorders.

Periodic Limb Movement Disorder and PTSD

PLMD is characterized by periodic highly stereotyped limb movements during sleep [17]. These movements, which occur primarily during non-REM sleep, are often associated with partial arousal or awakening [17]. PLMD is estimated to occur in 4 to 11 % of the general adult population [44]; however, its prevalence in individuals with PTSD is higher. Mellman and colleagues [4] found that 33 % of a group with PTSD had periodic limb movements that ranged from 2 to 33 per hour compared to 0 % in the healthy control group. Similarly, Ross and colleagues [45] and Germain and colleagues [46] found an elevated periodic limb movement index in PTSD patients compared to controls. To date, the highest prevalence of

clinically significant periodic limb movements in a PTSD population (76 %) was found in a group of Vietnam War Veterans [3]. The aforementioned studies had small sample sizes, and their findings are limited to combat-related PTSD (i.e., [4, 45]). However, the possibility that PLMD may contribute to the insomnia often endorsed by individuals with PTSD warrants further investigation. It also is important to keep in mind that antidepressant medications used to treat the PTSD symptom complex (see "Pharmacological Treatments for PTSD" below) can increase the incidence of periodic limb movements, and possibly exacerbate insomnia [47].

Rapid Eye Movement Sleep Behavior Disorder and PTSD

RBD is a parasomnia characterized by REM sleep without atonia on polysomnography and the enactment of REM sleep dreams [17]. Approximately 60 % of cases of RBD are idiopathic, although often the harbinger of a neurodegenerative disorder. RBD also can occur secondary to alcohol use and withdrawal and certain psychotropic medications, antidepressants in particular [17]. Although individuals with PTSD often report prominent, sometimes injurious, movement during sleep [8], and although there is much evidence for a fundamental REM sleep abnormality in PTSD [1, 48, 49], there are limited data on any relationship between RBD and PTSD. Husain and colleagues [5] reported that 56 % of a sample of RBD patients had comorbid PTSD. Additional studies are needed in order to better understand the phenomenology and comorbidity of RBD and PTSD. It also is important to keep in mind that antidepressant medications used to treat the PTSD symptom complex (see "Pharmacological Treatments for PTSD" below) can increase the incidence of RBD, and possibly exacerbate insomnia and recurrent nightmares [50].

Psychiatric Comorbidity in PTSD

In the National Comorbidity Survey, approximately 79 % of women and 88 % of men with PTSD had a lifetime diagnosis of at least one other psychiatric disorder [51]. The most prevalent comorbid diagnoses were depressive disorders, anxiety disorders, and substance use disorders [51–53], all of which are characterized by disturbed sleep. However, there are limited data on sleep in individuals with PTSD comorbid with another psychiatric disorder(s). In a national sample, Leskin and colleagues [10] found that PTSD/panic disorder patients, compared to individuals with PTSD alone, had a higher prevalence of nightmare (96 vs. 71 %) and insomnia (100 vs. 80 %) complaints. Further investigation is needed to examine

the extent to which sleep disturbance in PTSD is related to trauma exposure or a consequence of comorbid disorders.

Psychotherapeutic Interventions for PTSD

Several psychotherapeutic interventions for PTSD have been developed. The most widely recognized of these are cognitive behavioral therapies (CBT), including prolonged exposure therapy (PE) and cognitive processing therapy (CPT) [54]. Eye movement desensitization and reprocessing (EMDR) has also been recognized as a treatment for PTSD [54]. However, the Institute of Medicine (IOM) recommended exposure therapies as the only evidenced-based treatments for PTSD [55]. Several meta-analyses of the efficacy of psychotherapeutic interventions for PTSD have been published [56–59], but these rarely examined sleep outcomes [60]. The consensus is that there are large initial improvements in overall PTSD symptom severity [57], with greater effect sizes in studies with a higher proportion of women [57, 58], and small effect sizes in studies with mostly Veterans [57, 58]. There were no significant differences between active psychotherapies [59].

Some studies have considered the effectiveness of psychotherapy for PTSD in managing the associated insomnia and recurrent nightmares [61–65]. For the purposes of the current review, it is important to note that these sleep disturbances were frequently residual complaints following otherwise successful PTSD treatment [61]. Zayfert and DeViva [62] examined 27 patients from a rural tertiary care medical center who no longer met criteria for a PTSD diagnosis following CBT for PTSD. They found that 48 % of subjects reported residual insomnia, without persisting nightmares. Two small studies of flooding (arguably a variation of exposure therapy) in Veterans, neither of which focused on sleep and used validated sleep measures, had conflicting results [63, 64].

In one controlled EMDR study ($N=36$) that used an unvalidated nightmare measure and no insomnia measure, the nightmare disturbance improved following treatment [65]. Raboni and colleagues [66] found, in a small uncontrolled study, that, following treatment with EMDR, seven patients with PTSD exhibited an increase in sleep efficiency and a reduction in wake time after sleep onset; however, these findings may be the result of habituation over three nights as the first night PSG was used as a baseline measure. Galovski and colleagues [14] found that both PE and CPT were effective in reducing global sleep disturbance in adult female rape survivors; however, sleep impairment remained clinically significant in both groups despite an overall improvement in PTSD symptoms. Recently, Gutner and colleagues [15••] examined the long-term effects of CPT and PE on sleep disturbance. Similar to previous studies [14, 62], they found

significant improvements in waking PTSD symptoms but no remission of the sleep disturbance.

Taken together, the aforementioned studies indicate that existing treatments for PTSD are less effective in ameliorating the sleep disturbance than they are in treating the waking symptoms. Most studies were limited by small sample size, failure to use validated sleep measures, and lack of a control group. Thus, further investigation is required.

Cognitive Behavioral Treatment for Insomnia (CBT-I) in PTSD

To date, few studies have examined the efficacy of psychotherapeutic interventions for insomnia in individuals with PTSD. Cognitive behavioral therapy for insomnia (CBT-I) is a brief intervention aimed at improving overall sleep quality [67, 68]. It includes instruction in stimulus control and sleep restriction, cognitive restructuring, sleep hygiene education, and relaxation training [68]. Stimulus control is designed to limit negative associations with the bed and the bedroom [69]. Sleep restriction training aims to increase sleep drive and sleep efficiency by first limiting the amount of time spent in bed and then gradually increasing this time [69]. Cognitive restructuring identifies and challenges inaccurate beliefs and thoughts that directly interfere with sleep [69]. Sleep hygiene education discourages behaviors, such as alcohol consumption before bed, that interfere with healthy sleep [69]. Relaxation training, including progressive muscle relaxation, breathing exercises, and guided imagery, is designed to reduce the physical and/or mental tension that can delay sleep onset [69].

There is some evidence that CBT-I is efficacious for insomnia related to PTSD. DeViva and colleagues [70] studied five patients who responded to CBT for PTSD but continued to endorse insomnia symptoms. CBT-I was associated with a modest improvement in four of the five patients [70]. In another uncontrolled study of CBT-I in patients with PTSD ($N=$ 8), Gellis and Gehrman [71•] found significant improvements in self-reported sleep quality and the insomnia severity index (ISI) score, but no change in actigraphically measured sleep. Recently, Talbot and colleagues [72••] conducted the first randomized clinical trial of an 8-week course of CBT-I, provided individually, in a community sample being treated for PTSD. Compared to waitlist controls, the CBT-I group had a superior response on all sleep diary measures, on sleep quality assessed with the Pittsburgh Sleep Quality Index (PSQI), and on polysomnographically derived total sleep time; these effects remained significant at 6-month follow-up. Insomnia assessed with the ISI remitted in 41 % of the CBT-I group. However, both the CBT-I group and waitlist controls reported reductions in PTSD symptom severity and post-traumatic nightmares. Trials with an active treatment control group are required to establish the relation of these responses to the therapeutic elements of CBT-I specifically.

Psychotherapeutic Treatments for Nightmares in PTSD

Imagery rehearsal (IR; [60, 73, 74]) is the best studied psychotherapeutic intervention for recurrent nightmares. There is evidence that it leads to increased mastery of nightmare content and experience [75]. A variety of treatment protocols that share the following basic steps of IR have been studied: choosing a repetitive nightmare, rescripting it during waking, and imaginally rehearsing the new dream script at bedtime. IR treatment protocols differ widely in the type of nightmare to target for treatment, the extent of exposure to nightmare content, the individual guidance given by therapists to aid in rescripting, and the delivery format (individual or group) [76–78]. In addition, most forms of IR include additional potentially active treatment elements, such as CBT-I techniques.

Two recent meta-analyses statistically summarized the results of IR treatments for post-traumatic nightmares [74, 79], combining data from predominantly uncontrolled trials. They reported large effect sizes for nightmare frequency, sleep quality, and overall PTSD symptomatology. Casement and Swanson [79] also found that the effects were maintained at six and 12 months post-treatment. It is important to note that these meta-analyses combined results from a variety of treatment protocols and diverse post-traumatic populations (not necessarily diagnosed with PTSD), two important factors in treatment outcome [78].

Only two RCTs of IR for post-traumatic nightmares included potentially active control groups [80, 81]. In one study of Vietnam War Veterans with chronic, severe PTSD and recurrent nightmares [80], there was no significant difference in reducing nightmare frequency and PTSD severity and improving sleep quality between IR and a comparison treatment that incorporated elements of CBT-I. In the other RCT [81], both treatment groups (i.e., prazosin vs. behavioral sleep intervention), compared to a placebo control group, showed greater improvement in insomnia and PTSD severity. Harb and colleagues [78] have emphasized the limitations of the extant IR literature and identified strategies for advancing the field. In particular, Consolidated Standards of Reporting Trials (CONSORT) guidelines for conducting and reporting on trials should be followed in all clinical trials, and differences among treatment protocols and study populations be considered. Although not different from rates for other CBTs for PTSD [82], dropout rates for IR therapy range from 25 to 40 % [61]. It will be important to delineate the factors contributing to dropout as well as treatment success, as they may hold clues to optimizing the utilization of IR.

Exposure, relaxation, and rescripting therapy (ERRT) is a variant of IR that has shown promise for reducing nightmares and insomnia in predominantly civilian samples with post-traumatic symptoms [77, 83–85]. In an uncontrolled study in Veterans ($N=37$) that used imagery rescripting and exposure therapy (IRET), a variant of ERRT, Long and colleagues [86] showed reductions in nightmare frequency and PTSD severity and increased sleep time . Of interest for understanding the biological substrates of ERRT, Rhudy and colleagues [85] showed significant reductions with treatment in subjective and physiological (skin conductance, heart rate, facial electromyogram) reactions to nightmare-related content; these changes were maintained at 6-month follow-up.

Combined Psychotherapeutic Interventions for Insomnia and Nightmares in PTSD

Combining CBT-I and IR is intuitively appealing due to the prevalence of both insomnia and recurrent nightmares in PTSD. Accordingly, several integrated therapies have been developed. Krakow and colleagues [87] examined the efficacy of a combination treatment ("sleep dynamic therapy") in an uncontrolled study of 62 crime victims with PTSD. There were significant reductions in nightmares and PTSD severity and an improvement in sleep quality, but all outcome measures remained in the clinically significant range post-treatment. Crime victims treated with components of CBT-I and IR in a small uncontrolled trial showed a moderate improvement in sleep quality and a decrease in nightmare frequency, as well as a reduction in overall PTSD severity [88]. Veterans with PTSD, treated with components of CBT-I and IR in an uncontrolled investigation, had a reduction in insomnia, nightmare frequency, and nightmare distress [89]. In a recent meta-analysis of studies of CBT-I combined with IR, a large gain in sleep quality was reported; however, combined treatment did not significantly improve outcomes for PTSD severity and nightmares [79]. In summary, in the service of improving both the insomnia and nightmare problems related to PTSD, a combination of IR and CBT-I appears to be a promising treatment approach for many individuals.

Pharmacological Treatments for PTSD

The selective serotonin reuptake inhibitors (SSRIs) have the strongest evidence base among pharmacotherapies for PTSD [58, 90]. Two SSRIs, paroxetine and sertraline, are FDA-approved for this indication, although there is little evidence that they are superior to other medications of their class. The use of selective norepinephrine-serotonin reuptake inhibitors (SNRIs), in particular venlafaxine, is also supported by clinical guidelines [90]. However, there is remarkably little

evidence that insomnia and recurrent nightmares in PTSD respond to the SSRIs and SNRIs.

In a controlled trial of the SSRI sertraline for PTSD [91], the drug produced a 60 % response compared to 38 % with placebo; however, the change in the PSQI score was not greater with drug compared to placebo. In another trial [92], individuals receiving sertraline had a 53 % response rate compared to a 32 % placebo response; however, insomnia was the only adverse effect that occurred at a greater than placebo incidence. The SSRI paroxetine was reported to be effective for the acute treatment (12 weeks) of chronic PTSD, with a 62 % response rate compared to a 37 % placebo response; there was an improvement in all three PTSD symptom clusters; sleep quality was not assessed [93]. In a small open-label trial in Vietnam War combat Veterans, the SSRI fluvoxamine led to an improvement in "PTSD symptoms and all domains of subjective sleep quality" [94]. Of particular interest, dreams related to a combat trauma, which have been viewed as specific to PTSD [28], were reduced more than "generic unpleasant dreams" [94].

Although there is support from randomized controlled trials for the efficacy of the SNRI venlafaxine in treating PTSD, Davidson and colleagues [95] found no significant improvement in the hyperarousal symptom cluster, which includes insomnia. Stein and colleagues [96] did a pooled analysis of two randomized, double-blind, placebo-controlled trials and found no advantage of venlafaxine ER in reducing distressing dreams as assessed with the CAPS-SX17. Accordingly, the *Best Practice Guide for the Treatment of Nightmare Disorder in Adults* does not recommend venlafaxine for treating PTSD-associated nightmares [73].

The tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) have not been the subject of large randomized clinical trials for the treatment of PTSD [97]. There is only a low-level evidence for the usefulness of the TCAs in controlling recurrent nightmares [73]. Similarly, there is only a weak support for the usefulness of a MAOI, phenelzine, in ameliorating the nightmare disturbance in PTSD; this despite the prominent REM (rapid eye movement) sleep suppressant effect of the MAOIs and the evidence that most nightmares emerge from REM sleep [73].

The atypical antipsychotic drugs have been investigated as a treatment for PTSD. In a randomized placebo-controlled trial, individuals with non-combat-related PTSD treated with olanzapine monotherapy showed an overall greater reduction in the CAPS score, but only improvement in the Criterion C symptom cluster (avoidance and numbing) reached statistical significance [98]. Therefore, larger studies will be required to determine whether olanzapine alone can ameliorate the reexperiencing symptoms (including recurrent nightmares) and the hyperarousal symptoms (including insomnia) of PTSD. A small placebo-controlled trial of adjunctive olanzapine for combat-related PTSD non-responsive to SSRI

treatment found a greater improvement in sleep, as measured by the PSQI, in the olanzapine group [99].

Among the atypical antipsychotic drugs, the greatest number of randomized placebo-controlled trials for PTSD has been carried out with adjunctive risperidone [100]. Although the largest study, in Veterans, showed no significant effect [101], an advantage for risperidone in reducing the total CAPS score and the Criterion D scale score was found in another investigation of combat-related PTSD [102] and in a study of women with PTSD related to childhood abuse [103]. There have been no completed RCTs of quetiapine, ziprasidone, and aripiprazole in PTSD populations.

Pharmacological Treatments for Insomnia in Post-Traumatic Stress Disorder

Few studies have examined the benefits of pharmacotherapy for insomnia in individuals with PTSD [104]. Cates and colleagues [105] reported no significant advantage of the benzodiazepine clonazepam in a small, single-blind, placebo-controlled trial, which the investigators recognized as under powered. Clonazepam, the mainstay of pharmacological treatment for RBD [73], may have a place in the treatment of excessive movement during sleep in PTSD, a topic for future research.

In a series of case reports, the novel non-benzodiazepine benzodiazepine receptor agonist (NBRA) zolpidem was noted to be beneficial for insomnia related to PTSD [106]. In some cases, improvements in insomnia and nightmares were sustained for more than a year. In a randomized, double-blind, placebo-controlled trial, Pollack and colleagues [107•] found that a 3-week treatment with the NBRA eszopiclone led to greater improvements in PTSD symptoms including sleep disturbance.

The 5-HT$_2$ antagonist/SSRI trazodone, an antidepressant drug with prominent sedative properties, is often used in low doses for treating insomnia [108]. Combining trazodone with an SSRI is a common strategy for treating insomnia comorbid with depression [109]. Of a group of inpatients with PTSD, 80 % had been treated with trazodone, and of these, 72 % had found the drug helpful in decreasing nightmares and reducing the latency to sleep onset [110]. In a study of Vietnam War Veterans with PTSD, trazodone improved sleep, among a range of symptoms, after 2 to 3 months [111]. In a small group of individuals with war trauma-associated PTSD, nefazodone, another antidepressant that is a potent 5-HT$_2$ antagonist, led to a change in dream content from trauma- to non-trauma-related [112]. Although nefazodone is no longer widely used because of a concern about hepatotoxicity, this finding suggests that 5-HT$_2$ antagonism may be important in nightmare suppression.

Pharmacological Treatments for Nightmares in Post-Traumatic Stress Disorder

1As noted above, fluvoxamine, trazodone, and nefazodone may have some utility in treating the nightmare disturbance in PTSD. However, none of these drugs has been tested in a randomized controlled trial. Other drugs for which there is low level evidence of usefulness for recurrent nightmares are topiramate, low-dose cortisol, and gabapentin [73]. Several case series provide conflicting data on the benefit of cyproheptadine [73]. Arguably, the most important advance in the pharmacotherapy of the nightmare disturbance in PTSD has been the introduction of prazosin, an alpha-1 adrenoceptor antagonist that is FDA-approved for the treatment of hypertension in the U.S. Raskind [113] reported the first positive open-label trial of this drug in 2000. The first placebo-controlled trial of prazosin, carried out with a crossover design in U.S. military Veterans, reported a decrease in nightmares and an improvement in sleep quality [114]. A larger, placebo-controlled, parallel group study in Veterans with chronic PTSD confirmed the beneficial effect of prazosin in reducing nightmares and sleep disturbance [115]. A smaller placebo-controlled trial in civilians with PTSD also demonstrated an advantage of prazosin in reducing trauma nightmares [116]. Raskind and colleagues [117•] reported a decrease in combat-related nightmares in active-duty U.S. service members treated with prazosin compared to placebo; sleep quality and overall PTSD symptoms were improved as well. In a retrospective chart review study in Veterans with PTSD, prazosin led to a decrease in the number of non-nightmare-distressed awakenings, i.e., awakenings accompanied by extreme psychological distress without any recall of dream mentation [118].

1Prazosin is generally well tolerated. An alpha-1 adrenoceptor antagonist, it can be associated with light-headedness, orthostatic hypotension in particular. To minimize the latter problem, treatment is initiated at a dose of 1 mg hs, titrated upward every few days consistent with any reported side effects. The mean final dose in extant randomized clinical trials was in the range of 3 to 13 mg hs [114–116, 117•]. Individuals using a phosphodiesterase inhibitor for erectile dysfunction should be cautioned to separate the administration of the two medications by approximately 5 h in order to avoid additive hypotensive effects. Prazosin must be administered continuously to avoid the recurrence of nightmares; it is not known whether there could be a lasting beneficial effect after drug discontinuation.

It has been suggested that other drugs that reduce central noradrenergic activity might also ameliorate the nightmare disturbance in PTSD. There are positive case reports for clonidine, an alpha-2 adrenoceptor agonist that inhibits the firing

of noradrenergic locus coeruleus neurons. Clonidine was reported to be useful in treating post-traumatic nightmares in two Veterans with combat-related trauma [119], but no clinical trial of this drug has been conducted.

Conclusions

Chronic insomnia and recurrent nightmares are among the most distressing symptoms of PTSD, and evidence suggests that they are a core feature of the disorder [1, 61]. Other sleep disorders, including OSA, PLMD, and RBD, and other mental disorders may be comorbid with PTSD and have implications for successful treatment. Relatively few studies have directly investigated the effects of specific interventions on sleep disturbances in PTSD.

Psychotherapeutic interventions designed specifically to treat chronic insomnia and recurrent nightmares, CBT-I and IR, respectively, have shown promise and are considered first-line treatments. However, the majority of psychotherapy studies used some combination of CBT-I and IR, complicating efforts to identify the process by which each treatment achieves its effects. Better controlled studies that use a specific intervention and include an active treatment control group are needed to determine more definitively the efficacy of CBT-I and IR for the sleep disturbances in PTSD.

Pharmacological interventions for the overall PTSD symptom complex rarely have examined the efficacy of treatment for chronic insomnia and recurrent nightmares. Two SSRIs, paroxetine and sertraline, are FDA-approved for the treatment of PTSD; however, there is limited evidence that chronic insomnia and post-traumatic nightmares respond to these drugs. Although benzodiazepines are commonly prescribed for insomnia, they are not recommended due to the potential for dependence [120]. The alpha-1 adrenoceptor antagonist prazosin is the only pharmacological intervention for post-traumatic nightmares that received a grade of "recommended" by the AASM's best practice guidelines [73].

Compliance with Ethics Guidelines

Conflict of Interest Janeese A. Brownlow, Gerlinde C. Harb, and Richard J. Ross declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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A Critical Review of the Evidence Base of Imagery Rehearsal for Posttraumatic Nightmares: Pointing the Way for Future Research

Gerlinde C. Harb,[1] Andrea J. Phelps,[2] David Forbes,[2] Richard J. Ross,[1,3] Philip R. Gehrman,[1,3] and Joan M. Cook[4]

[1]Behavioral Health Service, Philadelphia VA Medical Center, Philadelphia, Pennsylvania, USA
[2]Department of Psychiatry, Australian Centre for Posttraumatic Mental Health, University of Melbourne, Melbourne, Australia
[3]Department of Psychiatry, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA
[4]Department of Psychiatry, Yale School of Medicine, and National Center for PTSD, West Haven, Connecticut, USA

In this article, the authors provide information on key characteristics of imagery rehearsal treatment protocols and examine the quality of reporting of randomized controlled and uncontrolled trials of imagery rehearsal for treating posttraumatic nightmares. Using a reliable and valid scale, two independent psychologists rated 16 trials. Most reports provided insufficient information on a range of variables including the definition of treatment delivery (e.g., therapist supervision, treatment fidelity), description of the participant sample, data analysis (e.g., determination of sample size), and treatment assignment (e.g., randomization procedures). Low methodological quality and poor reporting can lead to inflation of estimates of treatment effects and inadequately substantiated conclusions, such as inflated effect sizes in meta-analytic studies. Numerous imagery rehearsal protocols exist, but in some cases are given different names and tested in pilot studies, slowing progression in the field. Randomized controlled trials of imagery rehearsal with credible comparison conditions, examination of predictors of dropout and outcome, as well as dismantling studies of imagery rehearsal treatment components are needed.

Posttraumatic nightmares are a highly prevalent and distressing symptom for individuals who have experienced a traumatic event, particularly those with posttraumatic stress disorder (PTSD; Kilpatrick et al., 1997). Posttraumatic nightmares can contribute to significant sleep loss, poor sleep quality, daytime distress, and impaired functioning (Levin & Nielsen, 2007; Wittmann, Schredl, & Kramer, 2007; Zadra & Donderi, 2000). There has been growing interest in applying imagery rehearsal, a cognitive–behavioral treatment (CBT), to posttraumatic nightmares (for a general review, see Nappi, Drummond, & Hall, 2012). Imagery rehearsal is aimed at reducing nightmare frequency and intensity, and/or associated distress, and involves selecting a target nightmare, changing the storyline, and rehearsing the new dream (Marks, 1978).

A number of studies evaluating the efficacy of imagery rehearsal in traumatized populations have been conducted. Re-

cently, a meta-analysis statistically summarized imagery rehearsal research (Casement & Swanson, 2012), reporting large pre-post mean effect sizes (Lipsey & Wilson, 2001) for nightmare frequency ($ES_{WG} = 0.69$), sleep quality ($ES_{WG} = 0.68$), and PTSD symptoms ($ES_{WG} = 0.72$), and moderate to large effects for comparisons with control groups (nightmare frequency: $ES_{BG} = 0.59$; sleep quality: $ES_{BG} = 0.64$; PTSD symptoms: $ES_{BG} = 0.67$) for treatment completers. Importantly, this meta-analysis did not describe key characteristics of studies (e.g., treatment variations), nor did it take into account trial quality. Methodological quality includes the extent to which published reports contain sufficient detail about the design of the trial, the implementation of the protocol, and the presentation and interpretation of findings (e.g., Altman et al., 2001). The inclusion of trials with low methodological quality can alter meta-analytic estimation of treatment effects, inflating them up to 50% (Moher et al., 1998).

Standards for reporting clinical trials in the biomedical (Altman et al., 2001) and behavioral (Stinson, McGrath, & Yamada, 2003) research communities have been published with the currently accepted standard, the Consolidated Standards of Reporting Trials (CONSORT; Altman et al., 2001; Schultz, Altman, Moher, & Group, 2010). Although CONSORT has been extended to nonpharmacological trials (Boutron et al., 2008), some experienced psychotherapy researchers have

suggested that it fails to adequately assess factors specific to psychotherapy and developed a scale specific to such outcome studies (Kocsis et al., 2010).

The aim of the current investigation is to go beyond the statistical summary of outcomes towards a review of the methodologies of imagery rehearsal trials. Specifically, we describe differences among imagery rehearsal treatments (e.g., degree of exposure to nightmare content) and assess the reporting of the design and conduct of trials. Such information may be critical to understanding the current status of imagery rehearsal, the limitations of its efficacy, and future research directions.

Method

Study Inclusion

In this review, we include controlled and uncontrolled trials of imagery rehearsal for posttraumatic nightmares in adults. Trials with fewer than 10 enrolled participants were excluded, as were trials that did not focus exclusively on posttraumatic populations. A comprehensive bibliographic search was conducted along with a review of the study list in the Casement and Swanson (2012) meta-analysis. Eighteen trials were identified: 14 reviewed in the recent meta-analysis (Cook et al., 2010; Davis et al., 2011; Davis & Wright, 2007; Forbes, Phelps, & McHugh, 2001; Forbes et al., 2003; Krakow et al., 2000, 2002; Krakow, Johnston et al., 2001; Long et al., 2011; Lu, Wagner, Van Male, Whitehead, & Boehnlein, 2009; Moore & Krakow, 2007; Nappi, Drummond, Thorp, & McQuaid, 2010; Swanson, Favorite, Horin, & Arnedt, 2009; Ulmer, Edinger, & Calhoun, 2011) and four additional investigations (Germain et al., 2012; Harb, Cook, Gehrman, Gamble, & Ross, 2009; Krakow, Hollifield et al., 2001; Thunker & Pietrowski, 2012). For two trials with published interim reports, the more recent published report was examined (i.e., Forbes et al., 2003; Krakow, Hollifield et al., 2001).

Measures

The 16 trial reports were coded with regard to the following variables: treatment name, delivery, and dosage; instructions for choice of target nightmare; exposure to nightmare content; instructions for rescripting; and ancillary treatment elements. Other study design components were assessed: study population, history of prior trauma-focused therapy, percentages of women and participants with PTSD, sample size, control group, individuals enrolled as a percentage of those assessed for inclusion, and treatment dropouts.

The current study used the randomized controlled trial of the Psychotherapy Quality Rating Scale (RCT-PQRS; Kocsis et al., 2010), a validated instrument for assessing the quality of psychotherapy outcome trials (e.g., Thoma et al., 2012). This scale was constructed from the CONSORT Checklist and added items specific to psychotherapy trials (e.g., therapist training/supervision). It contains 25 items in six domains (for descriptions, see Table 3). Twenty-four items are rated on a

3-point scale ($0 = poor$, $1 = moderate$, and $2 = good$ execution and/or description), and the omnibus rating is scored on a 7-point scale (higher scores indicating better study quality and reporting). The scale provides a concise description for each rating, yielding measures of the completeness of description and the level of implementation of study elements in the published report. A number of items only apply to RCTs, and the rating/scoring procedure was adjusted accordingly for uncontrolled trials. Further, information on participant flow throughout trials (Stinson et al., 2003) was rated as present/absent.

Procedure

Two licensed clinical psychologists experienced in clinical trial methodology (GH and PG) independently rated the quality of the trial reports using the Kocsis et al. (2010) scale and additional participant flow items (Stinson et al., 2003). Ratings were made independently (Spearman's $\rho = .85$) for all trials, followed by a discussion resulting in consensus ratings for all items. Finally, design characteristics of trials (such as sample size and features of the intervention) were summarized.

Results

Table 1 lists the different treatment characteristics of imagery rehearsal protocols. The percentages reported below are out of the total number of trials that reported on this variable (see tables for totals). The core imagery rehearsal intervention across studies involved choosing a target nightmare, rescripting it and rehearsing a new dream, but protocols varied. Most trials (62.5%) delivered the treatment in groups, generally with an imagery rehearsal component of three to four sessions. The choice of the target nightmare(s) ranged from less intense, nonreplay dreams (24%) to the most distressing dream (25%); in 50%, the selection of nightmare was left entirely to the patient. Exposure to nightmare content was sometimes limited to patients choosing a nightmare and immediately changing it (31.3%), or it varied from writing the nightmare in detail and reading the script to the group and/or therapist (31.3%) to writing the nightmare in detail and also identifying trauma themes or aversive elements (37.5%). One study included one week of daily rehearsal of nightmare content.

Instructions for changing the nightmare differed from change the dream in "any way you wish" (31.3%) to making specific recommendations (37.5%), sometimes to address trauma-related themes (31.3%). The study protocols also varied in their inclusion of additional interventions. In order of frequency of use, these included elements of CBT for insomnia (Morin, 1993), relaxation (Miller & DiPilato, 1983), and imagery training (Laor et al., 1999).

The study methodologies are summarized in Table 2 (information not reported is indicated). The number of participants accepted as a percentage of those assessed ranged from 4% to 96%, with an average of 54.89% (standard deviation [SD] = 29.65). The mean dropout rate from uncontrolled trials was

Table 1

Variants of Imagery Rehearsal Used in Imagery Rehearsal Outcome Trials

Trial	Treatment name	Dosage	Format	Instructions for choice of target nightmare	Exposure to nightmare content	Instructions for rescripting nightmare	Additional treatment elements
Krakow, Hollifield et al., 2001	Imagery rehearsal therapy	2×3 hr $+ 1 \times 1$ hr	Group	Lesser intensity, not trauma replay	Write down nightmare	"Any way you wish"	Imagery skills
Krakow, Johnston et al., 2001	Imagery rehearsal therapy	10 hr 4 sessions	Group	Lesser intensity, not trauma replay	Write down nightmare	"Any way you wish"	Imagery skills CBT-I elements
Forbes et al., 2001, 2003	Imagery rehearsal therapy	6×1.5 hr	Group	War-related, weekly or greater frequency	Detailed write-out and read to group	Mastery/control; specific instructions how to rescript	PMR
Krakow et al., 2002	Imagery rehearsal therapy	6×2 hr	Group	Lesser intensity, not trauma replay	None	"Any way you wish"	Imagery skills CBT-I elements
Davis & Wright, 2007	Exposure, relaxation, rescripting therapy	3×2 hr	–	Trauma-related	Write out, read aloud, identify themes	Address identified trauma-related themes	PMR CBT-I elements
Moore & Krakow, 2007	Imagery rehearsal therapy	4×1 hr	–	–	–	–	–
Lu et al., 2009	Imagery rehearsal	6×1.5 hr	Group	War-related, weekly or greater frequency	Detailed write-out, read to therapist	Mastery/control; specific instructions how to rescript	–
Harb et al., 2009	Imagery rehearsal	7–8×1 hr	Individual	War-related, weekly or greater frequency	Detailed write-out, read to therapist	Mastery/control; specific instructions how to rescript	CBT-I elements PMR
Swanson et al., 2009	Modified exposure, Relaxation, rescripting therapy	5×1.5 CBT-I+ 5×1.5 EERT	Group	Worst, trauma-related	Write out, read, identify themes	Address identified trauma-related themes	PMR CBT-I elements
Cook et al., 2010	Imagery rehearsal	6×1.5 hr	Group	War-related, weekly or greater frequency	Detailed write-out, read to group	Mastery or control; specific instructions how to rescript	PMR

(Continued)

Table 1
Continued

Trial	Treatment name	Dosage	Format	Instructions for choice of target nightmare	Exposure to nightmare content	Instructions for rescripting nightmare	Additional treatment elements
Nappi et al., 2010	Imagery rehearsal therapy	4 × 1 hr or 4 × 2 hr	Individual or group	Military-related, weekly or greater frequency	None	"Any way you wish" with a positive ending	Imagery skills
Davis et al., 2011	Exposure, relaxation, rescripting therapy	3 × 2 hr	–	Trauma-related	Write, read, identify themes	Address identified trauma-related themes	PMR CBT-I elements
Long et al., 2011	Imagery rescripting, exposure therapy (IRET)	6 × 1.5 hr	Group	Most distressing and/or frequent	Write, read, identify themes, daily reading of nightmare	Address trauma-related themes	PMR CBT-I elements
Ulmer et al., 2011	Sleep intervention for PTSD (SIP)	3 × 1 hr imagery rehearsal + 3 × 1 hr CBT-I	Individual	–	None	Specific instructions on how to rescript, "Any way you like"	CBT-I elements Imagery skills
Germain et al., 2012	Behavioral sleep intervention (BSI)	5–8 × 45 min	Individual	–	–	–	CBT-I elements
Thunker, Pietrowski, 2012	Standardized nightmare therapy	3 × 50 min CBT-I + 5 × 50 min imagery rehearsal	Individual	Most distressing	Identify nightmare and aversive elements	Replace aversive elements while keeping dream content coherent	Sleep hygiene PMR Imagery skills

Note. CBT-I = Cognitive–behavioral therapy for insomnia; EERT = emotional energy release therapy; PMR = progressive muscle relaxation; – = information not reported.

Table 2
Imagery Rehearsal Studies in PTSD: Study Type and Characteristics

Trial	Study type	Control group	Sample size	Population	% PTSD diagnosis	% Women	Prior trauma focused treatment	Dropout rate: Enrollment to treatment completion (%)	Dropout rate: cumulative, enrollment to follow-up (%)	Percent enrolled from number assessed (%)
Krakow, Hollifield et al., 2001	RCT	Waitlist	168	Sexual assault survivors	–	100	–	25	41	83
Krakow, Johnston et al., 2001	Uncontrolled trial	none	62	Civilian violent crime survivors	100	84	–	–	–	–
Forbes et al., 2001, 2003	Uncontrolled trial	none	12	Vietnam veterans	100	0	Yes, all	0	0	–
Krakow et al., 2002	Uncontrolled trial	none	69	Fire survivors	56	61	–	4	15	–
Davis & Wright, 2007	RCT	Waitlist	43	Mixed civilian trauma survivors	67	82	–	26	26	–
Moore & Krakow 2007	Case series	None	11	Deployed active duty soldiers	–	–	–	0	–	–
Lu et al., 2008	Uncontrolled trial	None	17	Mixed veterans	100	0	No	12	18	29
Harb et al., 2009	Uncontrolled trial	None	11	Iraq veterans	100	0	No	27	36	–
Swanson et al., 2009	Uncontrolled trial	None	10	Vietnam, Gulf war veterans	100	0	–	20	–	44
Cook et al., 2010	RCT	Sleep/nightmare management	124	Vietnam Veterans	100	0	No	20	24	80
Nappi et al., 2010	Retrospective chart review	none	58	Mixed veterans	79	16	Variable	40	–	64
Davis et al., 2011	RCT	Wait list	47	Mixed civilian trauma	53	71	–	26	51	34
Long et al., 2011	Retrospective chart review	none	37	Vietnam and Gulf war veterans	100	0	Variable	11	–	–
Ulmer et al., 2011	RCT	Usual care	22	Mixed veterans	100	38	No	18	–	60
Germain et al., 2012	RCT	Prazosin, Placebo	57	Mixed veterans	58	9	–	35	37	4
Thunker & Pietrowski, 2012	RCT plus comparison with 2 added groups	Waitlist (+ depression and primary nightmare comparison)	69	Civilian outpatients	37	68	–	13	22	96

Note. – = information not reported; RCT = randomized controlled trial.

Table 3

Characteristics of Published Imagery Rehearsal Trials: Number Percentage of Trials Reporting Key Design Items (RCT of Psychotherapy Quality Rating Scale Ratings)

	Study quality rating																	
	Uncontrolled (n = 9)						RCTs (n = 7)						Total (n = 16)					
	0		1		2		0		1		2		0		1		2	
Item	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Description of participants																		
Diagnostic method, inclusion and exclusion criteria	3	33.3	6	66.7	0	0	0	0	4	57.1	3	42.9	3	18.8	10	62.5	3	18.8
Reliability of diagnostic methodology	5	55.6	4	44.4	0	0	1	14.3	6	85.7	0	0	6	37.5	10	62.5	0	0
Description of relevant comorbidities	6	66.7	2	22.2	1	11.1	5	71.4	1	14.3	1	14.3	11	68.8	3	18.8	2	12.5
Numbers of participants screened, included, excluded	6	66.7	0	0	3	33.3	1	14.3	2	28.6	4	57.1	7	43.8	2	12.5	7	43.8
Definition and delivery of treatment																		
Treatments described/referenced for replication	1	11.1	5	55.6	3	33.3	0	0	5	71.4	2	28.6	1	6.3	10	62.5	5	31.3
Treatment fidelity demonstrated	9	100.0	0	0	0	0	5	71.4	1	14.3	1	14.3	14	87.5	1	6.3	1	6.3
Therapist training/level of experience	1	11.1	6	66.7	2	22.2	3	42.9	2	28.6	2	28.6	4	25.0	8	50.0	4	25.0
Therapist supervision during treatment	5	55.6	3	33.3	1	11.1	5	71.4	1	14.3	1	14.3	10	62.5	4	25.0	2	12.5
Description of concurrent treatments	4	44.4	5	55.6	0	0	2	28.6	2	28.6	3	42.9	6	37.5	7	43.8	3	18.8
Outcome measures																		
Validated outcome measure(s)	2	22.2	5	55.6	2	22.2	1	14.3	2	28.6	4	57.1	3	18.8	7	43.8	6	37.5
Primary outcome measure(s) specified	0	0	5	55.6	4	44.4	1	14.3	2	28.6	4	57.1	1	6.3	7	43.8	8	50.0
Outcome assessment by blind raters/with reliability	8	88.9	0	0	1	11.1	3	42.9	4	57.1	0	0	11	68.8	4	25	1	6.3
Discussion of safety, adverse events	9	100.0	0	0	0	0	5	71.4	1	14.3	1	14.3	14	87.5	1	6.3	1	6.3
Assessment of long-term posttermination outcome	4	44.4	4	44.4	1	11.1	1	14	6	85.7	0	0	5	31.3	10	62.5	1	6.3
Data analysis																		
Intent-to-treat analyses	–	–	–	–	–	–	0	0	3	42.9	4	57.1	–	–	–	–	–	–
Description of dropouts and withdrawals	6	66.7	1	11.1	2	22.2	0	0	1	14.3	6	85.7	6	37.5	2	12.5	8	50
Appropriate statistical tests	0	0	7	77.8	2	22.2	0	0	6	85.7	1	14.3	0	0	13	81.3	3	18.8
Adequate sample size and power calculation	1	11.1	8	88.9	0	0	2	28.6	4	57.1	1	14.3	3	18.8	12	75.0	1	6.3
Appropriate consideration of therapist/site effects	9	100.0	0	0	0	0	6	85.7	0	0	1	14.3	15	93.8	0	0	1	6.3
Treatment assignment																		
A priori justification of comparison group(s)	–	–	–	–	–	–	1	14.3	3	42.9	3	42.9	–	–	–	–	–	–
Comparison group(s) from same population/time	–	–	–	–	–	–	0	0	0	0	7	100.0	–	–	–	–	–	–
Randomized assignment	–	–	–	–	–	–	0	0	3	42.9	4	57.1	–	–	–	–	–	–
Overall quality of study																		
Balance of allegiance to types of treatment	–	–	–	–	–	–	5	71.4	1	14.3	1	14.3	–	–	–	–	–	–
Conclusions justified by sample/measures/analyses	0	0	4	44.4	5	55.6	0	0	4	57.1	3	42.9	0	0	8	50.0	8	50.0

Note. For study quality ratings, 0 = inadequate description and/or inappropriate methods, 1 = adequate description and adequate method, 2 = full description and appropriate method. RCT = randomized controlled trial; – = not applicable.

17.4% ($SD = 14.81$), and from RCTs 33.4% ($SD = 11.45$). There was variation in the populations studied: 57.1% of trials included only participants with diagnosed PTSD; among the remainder, the percentage with a PTSD diagnosis ranged from 37 to 79%.

The number and percentage of reports meeting standards for the design and conduct of psychotherapy trials is presented in Table 3. The mean omnibus quality ratings on the RCT-PQRS were 3.14 ($SD = 1.22$), 4.1 ($SD = 1.22$), and 2.44 ($SD = 0.49$) for all trials, RCTs, and uncontrolled trials, respectively. Out of a possible 55 points, the mean total score for RCTs was 29.57 ($SD = 8.98$), ranging from 21 to 45. Among uncontrolled trials, the mean total score was 16.11 ($SD = 4.68$) out of a possible 45 points. The seven RCTs included predominantly waitlist or treatment-as-usual comparison groups (71.4%), with only two using potentially active controls. The randomization procedure was described completely in 57.1% of RCTs.

The participants were not fully described in most studies. Less than half of the studies reported complete information on participant selection (i.e., numbers assessed, eligible, enrolled, excluded). Of the seven RCTs, less than three quarters included a participant flow diagram similar to CONSORT guidelines. Although all RCTs included the number of participants randomized, 71.4% described how many participants were assessed, 85.7% how many were eligible, and 71.4% how many received an intervention. Only one trial stated the mean number of sessions received, but most included the number lost to follow-up. Participants' comorbidities and concurrent treatments were fully described by only 12.5% and 18.8% of trials, respectively.

The minority of studies described the treatment(s) in sufficient detail to allow replication. Although many included some information on the expertise and training of therapists, the supervision and assessment of treatment fidelity (i.e., therapists' adherence to the intended treatment) were rarely assessed. Half of the studies specified primary outcome measures, usually a large number ($M = 6.71$, $SD = 3.92$, range 2–15). Fifty percent provided a complete description of dropouts (85.7% of RCTs; 22.2% of uncontrolled trials). Only one investigation included a power analysis to justify the sample size.

Discussion

Despite the positive findings from a statistical summary of the results from randomized and uncontrolled trials of imagery rehearsal (Casement & Swanson, 2012), greater scrutiny of the characteristics and the quality of these trials and reports, as well as of fundamental differences among imagery rehearsal protocols, calls into question the strength of the current evidence base. It also raises questions about directions for future research.

Trial Quality and Reporting

RCTs remain the gold standard for demonstrating treatment efficacy (Persons & Silberschatz, 1998; Westen, Novotny, & Thompson-Brenner, 2004). Definitively establishing treatment efficacy requires the comparison of a group randomly assigned to a treatment with a group randomly assigned to a control condition (Schnurr, 2007). To control for nonspecific treatment variables (e.g., amount of therapist contact), the control treatment should be a potentially active treatment rather than inactive or waitlist (Schnurr, 2007). It is with an accumulation of such evidence that one can conclude that a treatment includes active ingredients that may improve upon those of other validated treatments. Of the 16 imagery rehearsal trials rated here, seven were RCTs, with only two comparing imagery rehearsal to an active comparison condition.

Detailed examination of imagery rehearsal trial reports indicates selection bias. The noninclusion of large proportions of assessed participants in combination with significant numbers of dropouts (ranging from 0 to 51% for nine studies that reported this number) may influence results and bias conclusions. Treatment completers may not be representative of a typical treatment-seeking posttraumatic population (Germain et al., 2012).

The reports often did not contain sufficient detail about essential trial characteristics including participant flow. Descriptions of treatment definitions and treatment delivery often lacked detail to allow for replication. Also, only one study included an independent measure of treatment fidelity, which would demonstrate that the treatment was delivered as intended. Many studies lacked descriptions of therapist training or supervision. Additionally, many studies did not report on participants' concurrent treatments and their prior participation in trauma-focused interventions. Consequently, it can be difficult to attribute symptom improvement to imagery rehearsal specifically, particularly in uncontrolled investigations.

It is difficult to determine from published reports whether investigators followed the recommended practice of specifying primary outcome measures in advance of data collection. Reports often referred to "outcome measures" in general, not distinguishing primary from secondary outcomes. Furthermore, studies tended to assess a large number of outcomes (6.71 on average); Altman and colleagues (2001) emphasize the importance of limiting primary outcomes to two to avoid problems of interpretation arising from multiple comparisons.

Important for the future of imagery rehearsal research are studies at the highest level of scientific rigor (adhering to CONSORT standards) that compare imagery rehearsal to a potentially active treatment control. In addition to establishing treatment efficacy, well-designed studies may provide valuable clinical information regarding differential treatment response, helping to identify trauma survivors who are most likely to benefit.

Variations in Protocols and Patient Populations

The treatments studied as imagery rehearsal for posttraumatic nightmares differ in the delivery of the core intervention, i.e., nightmare selection and rescripting. These differences may affect individuals' response to imagery rehearsal. For example, selecting less distressing and nonreplicative nightmares may lead to more symptom reduction. On the other hand, particularly if exposure to the original nightmare content may be a therapeutic ingredient, the opposite might be predicted. Determining how much exposure to include should be an important aim of future research (Moore & Krakow, 2010). At this point, it cannot be concluded that any particular imagery rehearsal protocol is preferred over others. Ideally, dismantling studies and comparisons of imagery rehearsal variants in RCTs will identify a particular protocol as most efficacious.

As in studies of PTSD (e.g., Bradley, Greene, Russ, Dutra & Westen, 2005), another potentially important difference among imagery rehearsal trials is the population studied, including the nature and chronicity of its posttraumatic symptoms. There is a wide range in the percentage of study participants with diagnosed chronic PTSD (37%–100%), likely resulting in different patient samples. This may be significant in light of the finding of Thunker and Pietrowski (2012) that patients with PTSD compared to others (depressed or idiopathic nightmare sufferers) showed a smaller treatment response. Another critical variable, reported by less than half of the trials, is previous trauma-focused treatment. For example, in Forbes, Phelps, and McHugh (2001), outcomes were almost universally positive for veterans who had received prior PTSD treatment; this contrasts with the less robust findings in treatment-naïve veterans (Lu et al., 2009).

The frequent combination of imagery rehearsal with other treatment methods, including CBT for insomnia (CBT-I), relaxation, and imagery skills practice is intuitively appealing, yet problematic for the outcome literature. As an example, a trial of imagery rehearsal combined with an evidence-based treatment such as CBT-I would be expected to show positive results based on the CBT-I component alone, in the absence of an alternative treatment control group. The Casement and Swanson (2012) meta-analysis found a significantly greater treatment effect on sleep quality for studies that combined imagery rehearsal with CBT-I. Without the benefit of dismantling studies or additive/constructive comparisons, it is difficult to evaluate the efficacy and essentiality of core imagery rehearsal treatment components. Furthermore, imagery rehearsal may benefit

from being viewed as one strategy in an overall treatment for posttraumatic sleep disturbance.

Further compounding the problem of variations in the treatment protocol, imagery rehearsal has been studied under seven different treatment names (see Table 1). Labeling a treatment variant with a new name means that the testing of the new intervention typically begins again at the lowest level of scientific rigor—a pilot study (e.g., Long et al., 2011). Such studies in isolation may not build on prior research and advance the field. Adopting a uniform treatment protocol would maximize the likelihood of identifying core imagery rehearsal treatment components that warrant dissemination to clinicians in the field.

Conclusions

The current review used a quantitative rating scale to evaluate the quality of the evidence base of imagery rehearsal. Although the scale was developed to rate RCTs, it was useful for rating uncontrolled trials as well. The conduct and reporting of uncontrolled trials may be improved by adopting common standards for design (e.g., monitoring treatment delivery) and reporting (e.g., providing detailed information about participants' comorbidities and concurrent treatments).

It needs to be acknowledged that the retrospective rating of outcome trials for study quality may not be able to distinguish problems in reporting from deficiencies in study design and conduct as study authors were not contacted for additional details about their procedures. This review is meant to encourage both scientific rigor in the design and conduct of future trials and clear reporting according to existing guidelines. As a result, consumers of research findings will obtain a more coherent and clear picture of the status of the evidence for the use of imagery rehearsal.

Finally, despite the existing evidence base for imagery rehearsal, researchers should remain open to the possibility that a treatment focused on posttraumatic nightmares may not be necessary or indicated. For example, one study investigating symptoms refractory to exposure therapy (Zayfert & DeViva, 2004) reported a low prevalence of nightmares, even among those who continued to experience insomnia. Furthermore, because an RCT of imagery rehearsal that used a potentially active control condition (Cook et al., 2010) found no superior effect of imagery rehearsal, it may emerge that effects detected in the uncontrolled studies are nonspecific and related to therapist support or monitoring.

It ought to be of help in investigating imagery rehearsal to delineate a theoretical rationale and a mechanism of action (e.g., exposure, mastery, conditioning, retrieval competition; Brewin et al., 2009; Krakow et al., 2000; Marks, 1978); none has yet been substantiated (Nappi et al., 2012). The single study that specifically examined a possible mechanism (Germain et al., 2004) found no association with treatment outcome.

In summary, interest in the use of imagery rehearsal to treat posttraumatic nightmares has been accompanied by the development and testing of various imagery rehearsal protocols.

To date, none of the treatment variants have been compared head-to-head to demonstrate superiority of any one protocol. Although all protocols share the core imagery rehearsal intervention, rescripting a nightmare and rehearsing the new dream, some have been given new names reflecting additional treatment components. Therefore, each variant is considered as a new treatment and tested in a pilot study, rather than building the evidence base for imagery rehearsal through higher-level study designs.

Future investigations should be aimed at conducting larger RCTs with credible comparison conditions and focused studies of mechanisms of action. Dismantling studies of elements of imagery rehearsal and ancillary treatment elements should lead to the identification of the core therapeutic components of imagery rehearsal and allow the field to move toward a more unified, yet flexible, approach to the treatment of posttraumatic nightmares. In addition, less restrictive inclusion and exclusion criteria would allow tests of imagery rehearsal for more naturalistic patient populations. It should be a goal of the field to identify patient factors that affect treatment acceptability, outcome, and dropout. Finally, the reporting of all trials should occur according to common guidelines. Although it is generally acknowledged that RCTs must be held to the highest standards, it should also be recognized that complete reports of well-designed uncontrolled trials could make a substantial contribution to the literature.

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Treatment of Nightmares in the Context of Posttraumatic Stress Disorder

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Philip R. Gehrman

University of Pennsylvania and Philadelphia VA Medical Center

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Gerlinde C. Harb

Philadelphia VA Medical Center

Nightmares are a common feature of posttraumatic stress disorder (PTSD) and are frequently resistant to treatment. Two emerging treatments for nightmares are pharmacotherapy with prazosin and psychotherapy using imagery rehearsal (IR). A case illustration demonstrates the application of these treatments with a client suffering from chronic, severe PTSD. The case illustrates the use of these strategies for managing PTSD-related nightmares, as well as the novel approach of scheduled awakenings following relapse. © 2010 Wiley Periodicals, Inc. J Clin Psychol: In Session 66:1185–1194, 2010.

Keywords: nightmares; sleep; PTSD; cognitive–behavioral therapy; REM; prazosin; imagery rehearsal

Nightmares commonly occur in the general population, and are often associated with substantial distress and impairment in daytime functioning. Individuals who suffer from posttraumatic stress disorder (PTSD) report high rates of nightmares, which are one of the current diagnostic criteria in the reexperiencing cluster of PTSD symptoms. Sleep disturbances and nightmares occur in the majority of individuals with PTSD, and it has been argued that nightmares are a hallmark symptom of PTSD (Ross, Ball, Sullivan, & Caroff, 1989; Wittmann, Schredl, & Kramer, 2007).

Until recently, it has been argued that nightmares, as a symptom of PTSD, would improve as the PTSD symptom complex improves with pharmacotherapy or psychotherapy. Although there is some evidence that nightmares improve following successful exposure therapy (Zayfert & DeViva, 2004), there is a need for other treatment options for clients who can not tolerate this form of treatment or for those with residual sleep problems. New treatments have therefore focused on nightmares as an important target in itself. The two main approaches studied in recent years

Correspondence concerning this article should be addressed to: Philip R. Gehrman, Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104; e-mail: gehrman@exchange.upenn.edu

have been the pharmacological agent prazosin and the cognitive–behavioral nightmare-focused imagery rehearsal (IR).

Prazosin

Prazosin is a novel and promising pharmacological treatment for posttraumatic nightmares, as well as non-nightmare-distressed awakenings (Thompson, Taylor, McFall, Barnes, & Raskind, 2008). It is a generic, non-sedating alpha-1 adrenergic antagonist that for many years has been prescribed to treat hypertension under the trade names of Minipress, Vasoflex, and Hypovase. Other alpha-1 adrenergic antagonists are routinely used in the treatment of benign prostatic hyperplasia, but prazosin is the only available drug of this class that crosses the blood–brain barrier, showing activity at central nervous system alpha-1 adrenergic receptors when administered peripherally. Alpha-1 adrenergic receptors are located in the hippocampus, amygdala, and prefrontal cortex; all of which have been implicated in the pathophysiology of PTSD. There is considerable evidence for noradrenergic hyperactivity in PTSD (Krystal & Neumeister, 2009). Although central noradrenergic tone is known to be significantly reduced during slow wave sleep and essentially absent during rapid eye movement (REM) sleep, there have been findings consistent with increased noradrenergic activity during sleep in patients with PTSD. Therefore, it has been hypothesized that prazosin acts centrally during sleep to reduce the nightmares and other events that lead to distressed awakening in patients with PTSD.

Two small double-blind placebo-controlled trials of the use of prazosin in military veterans have demonstrated promising outcomes in the reduction of posttraumatic nightmares (Raskind et al., 2003, 2007). These trials suggest that prazosin is substantially more effective than placebo for reducing nightmares in veterans with PTSD. In the larger trial (Raskind et al., 2007), a mean daily dose of 13 mg of prazosin (with several weeks of dosage adjustment) decreased recurrent nightmares by 50% as compared to 15% in the placebo group for treatment completers (33/40 participants). The onset of action of prazosin, the optimal prazosin dosage, and the appropriate length of treatment have not been determined to date; additionally, it appears prazosin must be continuously used and nightmares return readily after drug discontinuation (for review, see Taylor et al., 2008).

Other investigations of prazosin in the treatment of PTSD-related nightmares have resulted in case reports, chart reviews, and open-label trials. These reports indicate some clinical benefit of the treatment and suggest additional research will be essential to further elucidate the efficacy of this promising treatment. Several controlled trials are currently ongoing and hope to provide results from larger studies with diverse populations and from comparative trials of prazosin versus other nightmare-focused treatments (Miller, 2008).

Imagery Rehearsal

Imagery rehearsal is a promising method of cognitive–behavioral therapy (CBT) for PTSD nightmares. Although several forms of IR have been proposed, the patient always chooses a repetitive nightmare, changes its story line to make it less distressing and/or bring its story to a safe conclusion, and then mentally rehearses the changed dream imagery. One difference between various approaches to IR lies in the type of nightmare that is the focus of treatment. The approach presented in this case illustration allows the client to choose any target nightmare, in this case a nightmare that replayed aspects of the client's traumatic experience. When working

with replicative nightmares, the rehearsal of even a changed dream script likely entails a small degree of imaginal exposure. Other approaches involve the explicit focus on less-distressing and less-replicative nightmares.

A variety of studies have shown promise for IR as a treatment for posttraumatic nightmares (see review by Lancee, Spoormaker, Krakow, & van den Bout, 2008). Two randomized controlled trials have been published to date showing IR significantly reduced the frequency of nightmares in individuals with PTSD symptomatology and recurrent nightmares (Davis & Wright, 2007; Krakow et al., 2001). The treatment gains in nightmare frequency and distress were also maintained over time after treatment had ended. Although these are encouraging findings, these trials compared IR to wait-list comparison conditions, leaving room for the possibility that improvements were due to the nonspecific effects of being in any kind of psychotherapy. Furthermore, a significant proportion of participants did not meet full criteria for PTSD and/or had nightmares that were not necessarily related to their traumatic event. Uncontrolled investigations have also shown positive findings of IR in different populations.

Although the question of how daytime rehearsal of dream imagery may affect nighttime dreams has not been definitively answered through scientific investigation, several hypotheses have been proposed. Marks (1978) proposed that there are three active mechanisms of action of IR: exposure, abreaction, and mastery. Different versions of IR emphasize exposure/abreaction as the main therapeutic process (e.g., Davis & Wright, 2007), whereas others suggest that mastery over distressing dream elements may be the most active ingredient in IR (Germain & Nielsen, 2003). More recently, the retrieval competition hypothesis has been used to elucidate a potential avenue of action (Brewin et al., 2009). This theory suggests that different memory representations of the same event may compete for retrieval. Therefore, the rehearsal of an alternative, positive or neutral, image would make this new memory more accessible to retrieval than the imagery contained in the nightmare, making nightmares less likely to occur.

In short, multiple studies provide support for prazosin and IR as efficacious treatments for nightmares in clients with PTSD. Below we present a case illustration that demonstrates these two treatments along with a novel approach for managing nightmares.

Case Illustration

Presenting Problem and Client Description

"Brenda," a Caucasian woman in her mid-50s, presented to our sleep clinic because of longstanding difficulties with sleep and nightmares. She described a long history of mental health difficulties including PTSD, depression, and past alcohol and drug abuse. These problems, she believed, stemmed largely from her extensive history of sexual abuse by her father during her childhood. As an adult, she was again abused by her prior husband, exacerbating her difficulties. She had been in psychological treatment since her teenage years consisting of both psychotherapy and pharmacotherapy. She also reported several inpatient hospitalizations due to suicidality, with the most recent 3 years ago.

In regards to her sleep, Brenda reported considerable difficulty both with falling and staying asleep. At the time of intake, she took multiple medications at night including Seroquel and Klonopin to help promote sleep onset at her bedtime of approximately 10 p.m. She always awoke after 2 to 4 hours, almost invariably out of a nightmare.

Brenda described her nightmares as starting off as just "normal dreams" with unremarkable content. At some point in the dream her father and/or prior husband appeared and began to rape her. At this point in the nightmare, she usually woke up in a state of sustained highly heightened arousal, with racing heart and sweating. On most nights she could not get back to sleep for the rest of the night but stayed in bed trying to reinitiate sleep. On some nights she reported difficulty "shaking off" the nightmare but getting back to sleep, only to reenter the same nightmare.

Case Formulation

Brenda's pattern of nightmares is typical of clients with PTSD. As is so often the case in this population, her nightmares were resistant to various interventions over years of treatment. Many PTSD nightmares represent replays of the actual traumatic events the individual experienced. As such, the experience of the nightmare is also a reexposure to the traumatic events themselves. Thus, each time Brenda experienced a nightmare it represented a failed attempt at reducing the intensity of these emotional memories and may have actually increased the severity of her PTSD and associated comorbidities.

In addition, Brenda's nightmares also negatively impacted her sleep. A typical night of sleep is composed of several sleep cycles that each last around 90 minutes or so and repeat three to five times per night. Each cycle is characterized by a period of non-REM (NREM) sleep followed by REM. The first two cycles usually have more deep NREM sleep, which gradually decreases over the course of the night and is replaced by increasing amounts of REM sleep. Consistent with the view that REM sleep plays an important role in emotional processing, dreams with high affective content, including nightmares, typically arise out of REM sleep, although there is some evidence that PTSD-related nightmares may be a NREM phenomenon. Awakening from a nightmare is associated with the high sympathetic arousal characteristic of a fearful state, making it difficult to reinitiate sleep, resulting in impaired sleep in terms of quantity of hours slept. Brenda had therefore been in a state of constant sleep deprivation for many years and, in fact, could not remember her last good night of sleep. Consistent with this, she reported the typical consequences of chronic sleep loss, such as irritability, fatigue, and poor concentration. Sleep deprivation has also been shown to increase negative affect and to disrupt emotion-regulation processes (Yoo, Gujar, Hu, Jolesz, & Walker, 2007). As a result of this combination of sleep-related negative sequelae, Brenda's daytime functioning was impaired, further increasing her stress level and probably increasing the likelihood of experiencing a nightmare the following night. She was clearly stuck in a negative nightmare cycle that is unlikely to resolve on its own.

Course of Treatment

One of the interesting aspects of Brenda's case is that it illustrates a number of treatments for nightmares that were used at different points in treatment. Her treatment can be broken down into three phases based on the approach utilized.

Phase 1—Prazosin. When Brenda presented to the sleep clinic, her psychiatrist had recently started her on prazosin and was titrating her upwards to find a therapeutic dose. Her final dose was 9 mg per night. There was a dramatic reduction in the frequency of nightmares from nightly to one to two nightmares per week. This was the lowest nightmare frequency she had experienced in a number of years. On

nonnightmare nights she usually still woke up during the night but was able to get back to sleep in 30–60 minutes. Her total sleep time on these nights was in the range of 5 to 6 hours. Although still not an ideal sleep profile, it represented a significant improvement in Brenda's sleep. She also reported significant concomitant improvements in daytime functioning including reduced fatigue and sleepiness, greater ability to concentrate, and improved mood. It was not possible to determine how much of the sleep improvements were secondary to reductions in nightmares versus the direct effect of prazosin.

Phase 2—Imagery rehearsal. About 3 months into taking prazosin Brenda came to an appointment visibly depressed. She reported that her mood had worsened as a result of difficulties with her family. Further, her nightmares had returned on a nightly basis. Despite increases in the dose of prazosin, her frequent nightmares persisted. At this point we decided to initiate IR. For many clients the rationale behind IR can seem overly simplistic and thus treatment needs to be described carefully. Brenda was provided with an overview of IR and its rationale as follows:

> The goal of this technique called imagery rehearsal is to help you reduce the frequency and/or intensity of your nightmares. This is done by writing a new dream script that gives your mind a different place to go instead of those distressing images in your nightmares that wake you up. We will focus on one recurrent nightmare and together we will change the story line or some parts of the dream to make it less distressing, more like a normal dream. By practicing this new script, which reads more like a normal dream, in your imagination before you go to sleep, you can change your nightmares over time and this will help you wake up less often or be less upset when you do wake up. This therapy can also give you a chance to work with your nightmares in a safe environment. You can learn to master what happens in your dreams and use imagery to come up with safer and more positive dreams where you feel more in control. I know that most people are skeptical of this treatment initially; it is to be expected given that I am proposing to change your dreams that have bothered you night after night for so many years. It may seem difficult to accept that we can change what happens in our dreams while we are awake. I would like to get your reaction to this and discuss any questions you have about this technique.

After this description Brenda agreed to pursue this approach and stated that "at this point [she] would try anything." Brenda was given the homework assignment of selecting a repetitive nightmare that she wanted to make the initial focus of this approach.

At the next session we determined that most of her nightmares had the common traumatic ending of her father or ex-husband raping her and that she wanted to focus on this first. In session she was helped to write out a script of what occurs in a typical nightmare, including as much sensory and affective detail as possible. She became tearful while writing out the nightmare script, as is common when patients are asked to recount nightmares. After Brenda completed the nightmare script, she was asked to read it out loud. To help reduce emotional distress and arousal prior to the end of this session, a standard progressive muscle relaxation exercise was used.

In the following session, our goal was to generate a new version of the dream script that contained an altered, less-distressing ending and emphasized mastery and control. The client and therapist spent some time brainstorming possible ways to change the nightmare, as captured by the following dialogue:

Therapist (T): The goal is to change your nightmare in a way that makes it less distressing. There are a number of ways that people have chosen to change their nightmares. One option is to create an alternate ending that can even be unusual and creative. For example, you could even choose to sprout wings and fly away in the dream in order to escape a feared situation. Another option is to insert cues into the nightmare that serve as a reminder that it is only a dream and not reality. In your case, since your nightmares revolve around past abuse, you could take an object that reminds you of the present and add it to the dream. A third approach is to use what we call distancing techniques that change your nightmare from something you are experiencing to something that you are viewing from a distance. For example, you could change the script to be something you are watching on TV such that you then lower the volume of the TV and then turn it off altogether. There are many other possible ways to change your nightmare but this should give you some starting points. What are some possible ways you might want to change your nightmare?

Client (C): Well, I don't think I could go so far as to remove my father and ex-husband from the nightmare altogether because that seems like too much of a change to be convincing. I could change the dream so that I'm in a room that has a locked door. I know that my father or husband is outside of the door and they're trying to get in, but I know they don't have a key and have no way of opening the door. That would make me feel much safer.

T: That's a great suggestion for change. What other ideas do you have?

C: I like the idea of watching the nightmare as if it's on TV and then turning it off.

T: Do you think that would feel real enough to you?

C: I'm not sure. That may be too much of a change.

T: Can you think of any ideas that might even seem crazy to you?

C: What if I had Superman or some other superhero fly in to save me?

T: That's a creative option. You're free to change the script in whatever way seems best to you. Remember that because this is a dream anything can happen and you are not bound by the rules of reality.

As with any brainstorming, it is best to come up with a number of possible options. The client can then choose which change they want to make. In Brenda's case she chose to go with her first idea of using a locked door.

T: That seems like a good strategy for changing your nightmare. What I'd like you to do now is to write a new dream script, starting off like your typical nightmare, but this time incorporate the locked door into the script, using as much sensory and emotional details as possible. What sights, sounds, or other sensory details do you think would go along with this change?

C: Well, there's the obvious sight of the door.

T: What does it look like?

C: It's a brown door, plain. It's very sturdy, made with a strong wood like oak.

T: What other details can you think of?

C: It has a gold-colored doorknob, with a row of several strong locks above it. The locks are all locked and there are no keys to be found.

T: What do you think about the possibility of having you holding the keys in the new dream, so that you're in control of the situation?

C: I like that idea.

T: Can you think of any other sensory information?

C: I can hear the sound of them banging on the door and yelling to be let in. They're trying the doorknob but the door is too strong to be broken down.

T: What emotions would you feel in this situation?

C: On the one hand, I would be very scared knowing that they're trying to get into the room. On the other hand, there's a sense of safety and security knowing that they won't be able to get in.

T: In what ways would this make you feel safer?

C: There's a solid barrier between them and me. They can bang all they want but the door can't be broken down. I'm in a safe place and only I have the keys.

Brenda then wrote out a new version of the nightmare, incorporating this changed ending and its associated sensory and emotional content, emphasizing her mastery of the situation. She was asked to read out the new script once complete and we discussed whether she wanted to make any additional changes.

T: Now that you have your new nightmare script, what I want you to do is take the script home and read through it at night before you go to sleep. While you're reading the script imagine it in your mind and picture that you're experiencing it just as written. As you do this each night over the next week, one of several things might happen. You may not experience any change in your nightmare. You may continue to have the same nightmare, but it feels less intense or real. You may start to dream the new version of the nightmare. Or you may just experience fewer nightmares overall, either changed or not.

Brenda rehearsed the new nightmare script each night over the next few weeks. Gradually, she began to experience fewer nightmares, and those that did occur were less distressing. She had more success getting back to sleep after her nightmares, although it still usually took approximately an hour. She did not experience any changes in nightmare content. She expressed a great deal of relief from this change and felt that it was helping her mood as well.

Unfortunately, this trend toward improvement did not last very long. Brenda soon experienced some significant job stressors with the possibility of being laid off. As the stress increased, her nightmares returned in their full intensity. She continued to practice the script and even tried a new script, but her nightmares were no longer responsive to the altered imagery.

Phase 3—Scheduled awakenings. Brenda was feeling discouraged that her nightmares were back in their full intensity and were no longer responding to either IR or prazosin. Even after her stressful job situation came to a positive resolution, improvement in her sleep or nightmares did not follow. Her mood continued to be depressed, with some passive suicidal ideation. Her sleep was very disturbed but seemed to settle into a regular pattern. Brenda was still able to fall asleep at the beginning of the night with the help of her medications. She then woke up out of a nightmare 90 minutes after falling asleep. Subsequently, she stayed awake for about one hour, fell back to sleep, and had another nightmare approximately 90 minutes later. This seemed to be a consistent pattern that would recur two to four times per night, resulting in up to four nightmares per night. This regularity was likely a reflection of the 90-minute NREM–REM cycle. Based on Brenda's report it sounded as if every time she entered the REM portion of her sleep cycle she had a nightmare.

We decided to try a novel treatment approach that took advantage of the regularity in her pattern. This approach is referred to as scheduled awakenings and is

most often used for children who experience parasomnias such as sleepwalking or sleep terrors (Mindell et al., 2006). When these parasomnia behaviors occur with regularity, parents can intentionally wake their children earlier in the night with the hope of "breaking the cycle" and preventing the behavior from occurring. Once awoken the child is allowed to return right to sleep. We are not aware of any reports of scheduled awakenings being used in adults, but Brenda seemed to be a prime candidate and she agreed to try this approach given the predictable pattern of her nightmares.

Initially, only her first nightmare of the night was targeted. Because the first nightmare tended to occur 90 minutes into sleep, she set an alarm for 70 minutes after her anticipated time of falling asleep (fortunately, with the medications the length of time to fall asleep was also fairly predictable). Once she awoke to the alarm she was to turn it off and try to get back to sleep, with no other changes to her usual routine.

Brenda returned one week later reporting considerable success with scheduled awakenings. Each night her alarm went off prior to the onset of her first nightmare. She woke up, turned off the alarm, and was able to get back to sleep in 20 minutes or less. Rather than having a nightmare shortly after getting back to sleep, which would have been the anticipated timing based on her previous pattern, a nightmare did not occur until 90 minutes later. Thus she was having one less nightmare per night. It was then agreed that for the next week when she woke up to the alarm, she would reset it to go off in another 90 minutes (taking into account the time to fall back to sleep). After one week she reported that she was successful in reducing nightmares to only one or two per night. Although this is still a high frequency of nightmares, Brenda felt that this was a dramatic improvement and she was feeling much less distressed. She also thought that she was getting more sleep at night overall and felt more rested during the day.

Outcome and Prognosis

Brenda continued to practice scheduled awakenings, which successfully reduced her nightmare frequency, for a period of several months. She chose not to add a third scheduled awakening, and she felt reasonably well-rested during the day.

Since that time Brenda's nightmare severity and frequency has waxed and waned to some degree, usually depending on the severity of her depression. She has had a total of 15 sessions over the past 12 months and continues to be seen for treatment on a monthly basis. During periods of severe depression her nightmares typically worsened but then improved in parallel to changes in mood. Overall, she related significant improvement in her nightmares even though they were still occurring. It is unlikely that her nightmares will be eliminated unless the entire constellation of PTSD symptoms could be successfully treated. Despite a number of years of both psychotherapy and medication, her PTSD and depression have persisted. Her extensive abuse history suggests that her PTSD may be particularly difficult to treat and may endure along with some disturbed sleep and nightmares. The reduction, rather than the elimination, of impairing symptomatology may be a realistic goal.

Clinical Practices and Summary

The case of Brenda's nightmares is instructive in that it demonstrates several nightmare treatments for a woman suffering from severe PTSD-related nightmares. Successive treatment with prazosin, IR, and then scheduled awakenings was

demonstrated. These approaches still only constitute a limited repertoire of treatments for managing nightmares.

This case demonstrates several issues related to the treatment of PTSD nightmares that have clinical implications for treatment selection. First, PTSD nightmares most often begin as one of the symptoms of PTSD, and as such, often co-vary in severity or frequency with changes in PTSD or PTSD-related mood disturbances. Brenda's recent treatment history clearly demonstrated this exacerbation on her nightmares during times of increased stress or depressed mood. And, given the severity of her posttraumatic symptoms and depression, it is not surprising that it was during increases in other mental health symptomatology that treatment gains of the three treatment strategies were reduced or eliminated entirely. The severity and chronicity of her PTSD may indicate that a realistic approach would be to make small incremental changes in her sleep as her other posttraumatic symptoms hopefully improve.

Second, Brenda's case demonstrates that nightmares can be treated as a focal symptom separately from the more global PTSD, contrary to the general belief that successful treatment of nightmares is best accomplished by targeting the whole complex of PTSD. Brenda's PTSD severity did not appreciably change over the course of this sleep-focused treatment, but there were significant changes in nightmares and sleep as a result of targeted interventions. This suggests that treatments such as IR or scheduled awakenings are promising adjunctives that, when combined with PTSD treatments, may produce larger and more permanent clinical gains than either alone. Combined treatments for sleep disorders await testing in randomized clinical trials. In Brenda's case, past psychological treatment included a trial of prolonged exposure that did not alleviate either her nightmares or other PTSD symptoms.

In our work with IR we often find much greater long-term improvements in the frequency or distress associated with nightmares, even in clients with severe PTSD, than were achieved with Brenda. Her case was chosen because it demonstrates multiple strategies for treating nightmares in the same individual. However, regardless of the severity of PTSD, or even in the absence of PTSD, there are several evidence-based options available for the treatment of nightmares. Improving sleep and reducing nightmares can have a particularly positive impact on other domains of functioning in individuals with PTSD. Improved sleep likely enhances patients' mood and coping in general, and concentrations and motivation in particular, and may therefore augment the effectiveness of other PTSD treatments.

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Posttraumatic Nightmares and Imagery Rehearsal: The Role of Lucid Dreaming

Gerlinde C. Harb[1], Janeese A. Brownlow[1,2], Richard J. Ross[1,2]

Author Note

[1]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, Pennsylvania, USA; [2]Department of Psychiatry, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA

Please address all correspondence to: Gerlinde C. Harb, Ph.D., Corporal Michael J. Crescenz Veterans Affairs Medical Center, Research and Development Service (151), 3900 Woodland Avenue, Philadelphia, Pennsylvania 19104; Phone: 215-823-5800 x6128; Fax: 215-823-5171; email: gerlinde.harb@va.gov

Abstract

Lucid dreaming is a distinct behavioral state characterized by an awareness of dreaming while a dream occurs and, at times, an ability to control dream events and/or purposefully awaken from a dream. Lucid dreaming and its potential role as a mechanism of action of imagery rehearsal therapy (IR) were investigated in military veterans with posttraumatic stress disorder and recurrent nightmares. This study reports on thirty-three treatment-seeking Iraq and Afghanistan combat veterans participating in a larger clinical trial of six sessions of one of two therapies: *components of Cognitive-Behavioral Therapy for Insomnia (cCBT-I)* or *IR + cCBT-I*. Participants completed questionnaires regarding sleep and nightmares, other PTSD symptoms, and lucid dreaming before and after treatment. Before treatment, veterans demonstrated a lucid dreaming profile characterized by high dream awareness and low dream content control. After *IR + cCBT-I* treatment, lucid control of dream content increased more than after *cCBT-I* treatment (ES = 1.01). This increase in dream content control was related to a reduction in nightmare distress. An increase in a component of lucid dreaming, namely content control during ongoing dreams, may be one mechanism of change in imagery rehearsal therapy for recurrent posttraumatic nightmares.

Key words: imagery rehearsal, lucid dreaming, nightmares, posttraumatic stress disorder, sleep.

The state of lucid dreaming (LD) involves awareness, while a dream occurs, that one is dreaming and a capacity for metacognitive monitoring of an ongoing dream. It can be viewed as a hybrid state of consciousness, with features of both sleep and waking mental processes (Voss, Holzmann, Tuin, & Hobson, 2009). The identification of LD as a rapid eye movement (REM) sleep phenomenon, predominantly, is generally accepted (LaBerge, Nagel, & Dement, 1981). The study of LD has important applications for examining the nature of consciousness during sleep and for understanding and treating disturbances of normal sleep and dreaming, including the recurrent nightmares that characterize posttraumatic stress disorder (PTSD) (Doll, Gittler, & Holzinger, 2009).

The definition of LD has been broadened to include access to waking memories, capacity for future planning and ability to control dream content during dreaming, and purposeful waking from a dream (Voss, Schermelleh-Engel, Windt, Frenzel, & Hobson, 2013). LD can be assessed tri-dimensionally: dream awareness, dream content control, and control of waking from a dream. Additional LD constructs have been identified: insight, thought, dissociation (i.e., third person perspective), and positive emotion (Voss et al., 2013).

Estimates of the proportion of lucid dreamers in European population samples are 31-37% with rare (< one per month), and 20-30% with frequent (one or > per month) lucid dreams (Doll, et al., 2009; Blagrove, Bell, & Wilkinson, 2010). Lucid dreams represent only a small proportion of dreams. However, greater LD frequency has been related to better divided attention and mental health (Blagrove, Bell, & Wilkinson, 2010; Doll et al., 2009). Although a dream disturbance has been termed a hallmark feature of PTSD (Germain, 2013; Ross, Ball, Sullivan, & Caroff, 1989), LD has not been investigated in this disorder.

Therapies specifically designed to increase LD capacity recently have been reviewed (Stumbrys, Erlacher, Schädlich, & Schredl, 2012). One randomized trial of LD training as a treatment for idiopathic nightmares was negative; however, the brevity of the intervention and its self-help format were limitations (Lancee, Spoormaker, & van den Bout, 2010a). Spoormaker and van den Bout (2006) studied LD training, combined with other techniques, for predominantly non-trauma-related nightmares; they reported a reduction in nightmare frequency but could not ascribe the change exclusively to LD (Spoormaker & van den Bout, 2006). Whether posttraumatic nightmares would be responsive to a LD intervention has not been studied.

Imagery rehearsal therapy (IR), a form of cognitive-behavioral therapy, has garnered attention as a treatment for recurrent nightmares, in particular those of PTSD (Cook et al., 2010; Krakow et al., 2000). In IR, an identified target nightmare is rescripted during waking, and the changed dream is rehearsed imaginally before sleep. The mechanisms by which IR may reduce nightmare frequency and/or nightmare distress remain unclear; exposure, abreaction, and mastery have been proposed as therapeutic elements (Davis & Wright, 2007; Germain et al., 2004; Marks, 1978). Additionally, the imagery of the new dream script may compete with retrieval of the original nightmare (Brewin, Wheatley, Patel, & Fearon, 2009). We suggest that an increase in dream lucidity can occur in IR and enable the dreamer to transform a nightmare into an affectively neutral or positive experience.

The present study's goals were threefold. First, we aimed to describe three LD constructs (dream awareness, dream content control, purposeful waking from a dream) in a population of chronic nightmare sufferers with PTSD; we examined the relationships between LD and disturbed sleep and other PTSD symptoms. Second, we investigated changes in these constructs

with cognitive-behavioral treatment for posttraumatic nightmares, and the relationships of these changes to reductions in sleep and nightmare symptomatology. Third, we compared any effects on LD constructs of components of cognitive-behavioral therapy for insomnia (*cCBT-I*) and an IR intervention plus *cCBT-I* (*IR + cCBT-I*). We hypothesized that only the IR-containing treatment would enhance LD and that this increase in LD would be associated with a reduction in nightmare symptoms.

Method

Participants

The 33 participants (including seven women) were a subset of American Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) veterans enrolled in a large randomized controlled trial (RCT) comparing two cognitive-behavioral treatments for recurrent posttraumatic nightmares, *cCBT-I* and *IR + cCBT-I* (clinical trials registration number: clinicaltrials.gov NCT00691626). LD was investigated during two of the recruitment years, and approximately one third of the RCT enrollees were administered LD questionnaires. Of the 33 participants, 26 completed one of the two treatments and were included in pre- to post-treatment change analyses. Of the seven non-completers, five dropped out before the start of treatment and two during treatment. The participants in the two groups were comparable, with no significant differences in baseline demographic or clinical characteristics (see Table 1, all *p* values > .05).

Participants in the RCT were enrolled in mental health care at the Corporal Michael J. Crescenz VA Medical Center (CMCVAMC) in Philadelphia, Pennsylvania, USA or one of its outpatient clinics. They had current PTSD, assessed with the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995) by an independent assessor blind to treatment assignment,

deployment-related recurrent nightmares (minimum frequency: one every two weeks for six months), and a global sleep disturbance as assessed by the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). They were allowed to engage in concurrent non-sleep-focused treatments (psychotherapy and pharmacotherapy), and medication regimens were stable for at least two weeks prior to entry into the study. Participants with comorbid major depression, DSM-IV anxiety disorders other than PTSD, or alcohol or cannabis abuse (as assessed with the SCID for DSM–IV; First, Gibbon, Spitzer, & Williams, 2001) were included in the RCT. Exclusion criteria were: schizophrenia and other psychotic disorders, bipolar disorder, severe traumatic brain injury (loss or alteration of consciousness greater than 24 hours or peri/post-traumatic amnesia greater than 7 days), current substance dependence, and evidence for "at risk" drinking.

Measures

The Lucid Dreaming Subscale of The Iowa Sleep Experiences Survey (ISES-LD; Watson, 2001) is a self-report measure with three LD construct items (awareness of dreaming, control of dream content, and ability to self-arouse from dreams) rated on a 7-point Likert scale (1 = *never* to 7 = *several times a week*). The scale has demonstrated validity and acceptable reliability, with coefficient alphas from .75 to .78 (Watson, 2001).

The Nightmare Frequency Questionnaire (NFQ; Krakow et al., 2000) is a self-report questionnaire with two measures of nightmare frequency: 1) number of nights with one or more nightmares per week, and 2) total number of nightmares per week. Test-retest reliability between retrospective and proximal reports was high (Krakow et al., 2000).

The Nightmare Distress Questionnaire (NDQ; Belicki, 1992) is a reliable and valid self-report measure of the intensity of distress associated with nightmares. It contains 13 questions

rated on a 5-point Likert scale, summed to create a total score.

The PSQI (Buysse et al., 1989) is a 19-item self-report instrument that assesses global sleep disturbance. The items generate seven subscales: sleep quality, latency, duration, efficiency, and disturbance, hypnotic medication use and daytime dysfunction. Each subscale is scored on a 0 to 3 scale, yielding a global score from 0 to 21. A global score greater than 5 indicates poor sleep, with good sensitivity and specificity. Internal consistency (α =.83) and test-retest reliability (r = .85) are satisfactory.

The PTSD Checklist-Military (PCL-M; Blake et al., 1995) is a 17-item reliable and valid self-report inventory of the 17 DSM-IV criteria for PTSD. Using a 5-point scale (1 = *not at all* to 5 = *very often*), individuals indicate the extent to which they have experienced each symptom in the past month.

Procedure

The study was approved by the CMCVAMC Institutional Review Board, and participants provided written informed consent. The five self-report measures were administered at baseline, prior to the intervention (N = 33), and within one week after its completion (N = 26). Both treatments were provided in six weekly, hour-long individual sessions by doctoral level psychologists. The techniques employed in *cCBT-I* were psychoeducation about sleep hygiene, sleep problems in PTSD, and the effects of stress on sleep; and instruction in stimulus control, progressive muscle relaxation, and methods for reducing cognitive hyperarousal. *IR + cCBT-I* included, in addition, the elements of IR treatment (Forbes, Phelps, & McHugh, 2001; Harb, Cook, Gehrman, Gamble, & Ross, 2009), i.e., writing the content of a detailed recurring nightmare of the participant's choice, brainstorming for potential changes, and composing a new dream script to practice nightly before sleep (imaginal rehearsal). Suggested changes in dream

scripts included devising an alternative ending, inserting reminders that the dreamer survived

dream events and/or that she/he is only dreaming, and distancing self from the dream's action by

becoming an observer.

Data Analysis

Descriptive and inferential statistics for all measures were computed using IBM SPSS

version 21 (no missing data). Baseline LD construct frequencies were calculated using all 33

participants. Chi-square tests and t-tests were used to compare group differences on

demographics and clinical measures. Pearson correlations were examined to determine

relationships of LD to other clinical characteristics. Linear mixed modeling (LMM) was

employed to analyze treatment effects for each LD construct. The fixed effects in the analyses

were treatment condition (*IR + cCBT-I* vs. *cCBT-I*), time (baseline vs. post-treatment), and the

two-way interaction of treatment condition and time.

Results

Baseline descriptives

The correlations between baseline LD and other baseline variables were examined. The

LD constructs (awareness, content control, purposeful waking) demonstrated no significant

relationships with nightmare frequency ($r = .08, p = .674; r = .00, p = .995; r = .21, p = .238$),

nightmare distress ($r = -.20, p = .252; r = -.09, p = .630; r = -.02, p = .927$), PTSD severity ($r = -.18, p = .311; r = -.16, p = .382; r = .12, p = .509$), or global sleep disturbance ($r = -.01, p = .937; r = -.09, p = .603; r = -.10, p = .569$).

More than a third of participants reported frequent awareness of ongoing dreams, but

only 9% endorsed frequent dream content control (Table 2). Dream awareness occurred, on

average, several times a year (*mean* = 3.65, *SD* = 2.07, *range*: 1-7); content control, on average,

less than once a year (*mean* = 1.96, *SD* = 1.37, *range:* 1-5); and purposeful waking, on average, once or twice a year (*mean* = 3.38, *SD* = 1.77, *range:* 1-7).

Changes with treatment

Participants in the two treatment groups were compared. There were no significant treatment condition by time interaction effects on awareness, content control, or purposeful waking ($F(1,48)$ = .00, p = 1.00, ES = .52; $F(1,48)$ = 1.14, p = .290, ES = 1.01; $F(1,48)$ = .19, p = .665, ES = .53). The large interaction effect size for content control (ES = 1.01) was examined in more detail (see Figure 1). Follow-up pairwise comparisons demonstrated significantly greater change in content control for participants in the *IR+cCBT-I* group compared to the *cCBT-I* group, *mean (SD)* = 2.92 (.31) vs. 1.62 (.31), respectively, p = .004. There were no main effects of time and treatment condition on awareness (time: $F(1, 48)$ = .02, p = .897; treatment: $F(1, 48)$ = 3.82, p = .057) or purposeful waking (time: $F(1, 48)$ = .19, p = .665; treatment: $F(1, 48)$ = 2.55, p = .117). There was no significant main effect of time on content control, $F(1, 48)$ = 2.03, p = .161; however, the main effect of treatment was significant, $F(1, 48)$ = 9.18, p = .004, with increased content control in the *IR+cCBT-I* group compared to the *cCBT-I* group.

For the *IR + cCBT-I* group only, the increase in dream content control was strongly and significantly related to decreased nightmare distress (r = .77, p = .002). Overall, the increase in content control with treatment demonstrated medium to large correlations with decreases in nightmare frequency (r = .34, p = .092), nightmare distress (r = .34, p = .086), and general sleep disturbance (r = .46, p = .116).

Discussion

In this first study of the phenomenology of LD in individuals with chronic PTSD and recurrent nightmares, a sample of OEF/OIF/OND veterans reported one LD construct, frequent

awareness of ongoing dreams, more commonly than previously described in non-clinical population samples (Doll et al., 2009; Schredl & Erlacher, 2011). Interestingly, frequent dream content control was particularly rare in our participants (9% of the total number, or 13% of those who endorsed dream awareness). Previous survey research in a child and adolescent population found that 37% of lucid dreamers were regularly able to change or control events in their dreams (Voss, Frenzel, Koppehele-Gossel, & Hobson, 2012); however, this is likely an overestimate of adult lucid dream control as LD experiences, generally, are reported to be more common in children and adolescents (Voss et al., 2012). Nonetheless, individuals with PTSD and recurrent nightmares appear to demonstrate a particular LD profile, namely increased awareness of ongoing dreams coupled with low control over dream content. The combination of conscious awareness of dreaming and inability to control the dream plot may contribute to the particularly distressing nature of posttraumatic nightmares, which often replicate a traumatic event (Esposito, Benitez, Barza, & Mellman, 1999).

The frequency of LD experiences prior to treatment with *cCBT-I* or *IR+cCBT-I* was not associated with PTSD severity or overall sleep quality. This is broadly consistent with limited previous research, which has found that, although LD was generally related to better overall mental health, it was not associated with reduced anxiety symptomatology (Doll et al., 2009; Schredl & Erlacher, 2004; Spoormaker, Bout, & Meijer, 2003). In addition, the two studies of LD training for PTSD symptomatology (in individuals without diagnosed PTSD and mostly idiopathic nightmares) showed no change in PTSD symptom severity (Lancee, van den Bout, & Spoormaker, 2010b; Spoormaker & van den Bout, 2006).

The American Academy of Sleep Medicine recommends IR for the treatment of idiopathic nightmares and notes that IR appears to be effective for treating the nightmares

associated with PTSD, in civilians in particular (Aurora et al., 2010). Outcomes with combat

veterans have been less positive (Cook et al., 2010; Harb et al., 2013), and insight into the

therapeutic mechanism of IR would likely help in understanding different responses to this

treatment. Because lucid dreams in general population samples tend to be characterized by a

strong sense of control over dream content (Gackenbach & LaBerge, 1988; Wolpin, Marston,

Randolph, & Clothier, 1992), and because IR involves the conscious rescripting of a nightmare,

we hypothesized that one way in which IR reduces nightmare-related distress is by enhancing the

capacity for lucid control of dream content. More precisely, we expected that IR specifically,

and not the more general treatment of sleep disturbance, *cCBT-I*, would effect changes in LD

constructs.

Overall, we did not find statistical significance for differences in changes in LD

constructs between participants randomized to the two types of treatments. However, this may be

attributable to low power for the linear mixed modeling analyses. Exploratory comparisons

showed that, with *IR+cCBT-I,* participants demonstrated significantly larger increases in lucid

dream content control than with *cCBT-I* (see Figure 1)*.* This finding builds on previous research

showing that IR may encourage general feelings of active mastery by including mastery elements

in new dream scripts (Germain et al., 2004).

An indication of the clinical importance of enhanced dream content control, which

previously has been associated with increased general well-being (Wolpin, Marston, Randolph,

& Clothier, 1992), is our finding that it was correlated with a decrease in nightmare distress.

There was no correlation with a change in nightmare frequency; however, nightmare distress and

nightmare frequency are thought to represent orthogonal axes of dream description. Compared to

nightmare frequency, nightmare distress may have a stronger relationship to psychopathology

and may independently show a response to treatment for nightmares (Cook et al., 2010).

With the enhancement of dream content control as one possible mechanism of action of

IR, a therapy without explicit LD training, it is important to consider the extant literature on LD

therapy for nightmare disturbances. Although not studied rigorously as a treatment for

posttraumatic nightmares, LD training for the management of nightmares has been reported in

case studies (e.g., Spoormaker et al., 2003) and in three randomized trials with predominantly

idiopathic nightmare sufferers (Holzinger, Klösch, & Saletu, 2015; Lancee et al., 2010b;

Spoormaker & van den Bout, 2006). Holzinger and colleagues (2015) added LD training to

Gestalt therapy for idiopathic nightmares and found equivalent significant reductions in

nightmare frequency in both groups; LD frequency increased significantly with LD training.

Whether the response to IR treatment can be enhanced by incorporating specific LD training

deserves to be examined.

In conclusion, we suggest that the essential element of IR, the creation and rehearsal of

new, alternative dream imagery, may enable the nightmare sufferer to achieve greater control of

otherwise immutable, highly distressing posttraumatic nightmares, in part by promoting lucid

dream control. A focus on LD may hold promise for several clinical applications: elucidating the

pathophysiology of the dream disturbance in PTSD; explaining how IR successfully treats some

nightmare sufferers with PTSD; and developing improved treatments for recurrent posttraumatic

nightmares. Recently, Voss and colleagues (Voss et al., 2014) demonstrated that fronto-temporal

transcranial alternating current stimulation (tACS, 25 or 40 Hz) during REM sleep could induce

LD in healthy young adults with no previous LD experience, and they suggested that tACS

during REM sleep in individuals with PTSD could be used to change the content of nightmares.

We propose that adding tACS to IR treatment could be studied as a means of increasing the response to IR.

Several limitations of the current study should be noted. First, its generalizability may be limited because the study population included only treatment-seeking military veterans with PTSD who identified recurrent nightmares as a significant problem. Their LD profile may differ from that of other traumatized populations with a nightmare disturbance. Second, the self-report ISES-LD does not distinguish an increase in control over dreams generally from nightmares in particular. Therefore, future research should expand the assessment of LD constructs to include the evaluation of lucid nightmares specifically. It also would be important to utilize the newly developed Lucidity and Consciousness in Dreams Scale (LuCid; Voss et al., 2013) to expand the assessment of the range of LD constructs. Finally, the sample studied in this investigation is small, resulting in limited statistical power, and our findings should be replicated in a larger sample.

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Table 1

Baseline Demographic and Clinical Characteristics

	All veterans, baseline (n=33)	IR+cCBT-I (n=13)	cCBT-I (n=13)	Group comparisons[†] χ^2 or t
Age (mean years, *SD*)	37.91 (10.60)	40.46 (11.54)	36.08 (10.70)	1.01
Gender (% of total)				.25
Male	78.8	84.6	76.9	
Female	21.2	15.4	23.1	
Race (% of total)				1.41
Caucasian	45.5	53.8	38.5	
African American	51.5	46.2	53.8	
Other	3.0	0.0	7.7	
Marital Status (% of total)				2.60
Married/partnered	45.4	46.2	46.1	
Never married	30.3	23.1	38.5	
Separated/divorced	24.3	30.7	15.4	
Education (% of total)				2.22
High school	24.2	30.7	23.1	
Some college	51.5	46.2	61.5	
College degree	21.2	15.4	15.4	
Graduate degree	3.1	7.7	0.0	

Employment (% of total)				7.28
Full-time	27.3	30.7	23.1	
Part-time	21.2	23.1	23.1	
On disability	15.1	23.1	0	
Unemployed/retired/other	36.4	23.1	53.8	
Clinical characteristics (mean, SD)				
Nightmares/week (NFQ)	5.0 (3.6)	5.08 (4.82)	4.92 (2.84)	.10
Nightmare distress (NDQ)	30.70 (4.90)	30.85 (4.76)	30.15 (5.90)	.33
PTSD severity (PCL-M)	66.91 (8.56)	67.84 (6.87)	65.08 (9.97)	.83
Global sleep disturbance (PSQI)	15.24 (2.74)	15.62 (2.87)	15.23 (2.49)	.37
Lucid awareness (ISES)	3.6 (2.1)	4.2 (1.9)	3.1 (2.1)	1.45
Lucid dream control (ISES)	2.1 (1.5)	2.4 (1.6)	1.5 (1.0)	1.63
Purposeful waking (ISES)	3.2 (1.8)	3.7 (1.8)	3.1 (1.8)	.88

Note. † Group comparisons by treatment assignment, all comparisons $p > .05$. NFQ = Nightmare Frequency Questionnaire; NDQ = Nightmare Distress Questionnaire; PSQI= Pittsburgh Sleep Quality Index; PCL-M = PTSD Checklist-Military, ISES= Iowa Sleep Experiences Survey.

Table 2

Frequency of LD Experiences in Veterans with PTSD and Recurrent Nightmares.

	None	Rare	Frequent
Dream awareness (% of total sample)	27	33	40
Dream control (% of total sample)	55	36	9
Purposeful waking (% of total sample)	24	55	21

Note: None = no LD experience; Rare = a LD experience less than once a month; Frequent = a

LD experience once a month or more often (Schredl & Erlacher, 2004).
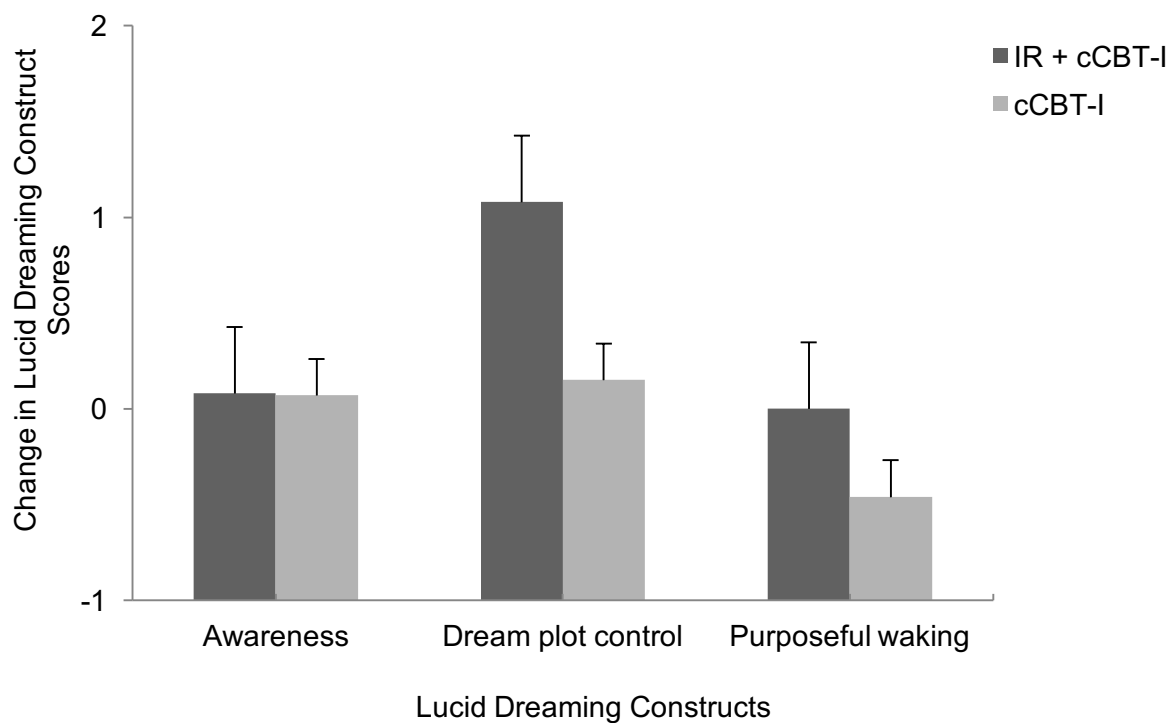
Figure 1.

Lucid Dreaming Baseline to Post-Treatment Change Scores as a Function of Treatment Group

Treatment of Sleep Disturbance in U.S. Veterans with PTSD:

Nightmare-focused and Insomnia-focused Treatments, Treatment Moderators, and the Effects of Neurocognitive Functioning.

Treating Posttraumatic Sleep Disturbance in U.S. Veterans Who Served in Iraq and Afghanistan: Findings from a Randomized Controlled Trial

Gerlinde C. Harb [1]
Joan Cook [2]
Andrea Phelps [3]
David Forbes [3]
Philip Gehrman [1,4]
Ilan Harpaz-Rotem [2]
Russell Localio [4]
Mark Cary [4]
Richard J. Ross [1,4]

Institutions: [1] Michael J. Crescenz VA Medical Center, Philadelphia, PA; [2] Department of Psychiatry, Yale University, New Haven, CT; [3] Phoenix Australia, University of Melbourne, Melbourne, Australia; [4] Department of Psychiatry, University of Pennsylvania, Philadelphia, PA

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Boston University School of Medicine asks all individuals involved in the development and presentation of Continuing Medical Education (CME) activities to disclose all relationships with commercial interests. This information is disclosed to CME activity participants. Boston University School of Medicine has procedures to resolve apparent conflicts of interest. In addition, presenters are asked to disclose when any discussion of unapproved use of pharmaceuticals and devices is being discussed.

I, Gerlinde Harb, have no commercial relationships to disclose.

Purpose of this Presentation

- Present the design and primary outcomes of a randomized controlled trial (RCT) of Imagery Rehearsal therapy (IR) for recurrent PTSD-related nightmares in male and female OEF/OIF/OND Veterans
  - Large trial (n=108)
  - Very symptomatic sample
  - Active comparison condition

Imagery Rehearsal Therapy - Background

- Recognition of the importance of sleep and nightmare symptoms in PTSD
  - 70-90% of patients with PTSD report a nightmares, nightmares predict later PTSD
  - Sleep symptoms including nightmares often remain a clinically significant residual problem for PTSD treatment completers
  - Need for nightmare-focused treatments
- What is Imagery Rehearsal therapy (IR)?
  - A cognitive-behavioral treatment (CBT) that directly addresses recurrent nightmares by
    - Revising the story line of a nightmare during waking
    - Encouraging the rehearsal of the new (non-distressing) dream script before bedtime
- Variations (EERT, IRT, IR, sleep-dynamic therapy, etc.)
  - Selection of the targeted nightmare
  - Amount of exposure to nightmare content
  - Addition of components of CBT for Insomnia (CBT-I)

State of IR Research

- Meta-analyses (Augedal et al., 2013; Casement and Swanson, 2012; Hansen et al., 2013)
  - Average reductions in nightmare frequency, sleep quality, and overall PTSD moderate to large, effects maintained at six and 12 months post-treatment
- Caveats (Harb et al., 2013)
  - Predominantly uncontrolled or wait-list controlled studies
  - Heterogeneity of samples, treatment characteristics
- Civilian trauma survivors vs. Veterans
  - Differ from populations sampled in most IR trials:
    - tend to be predominantly male and with diagnosed, often severe PTSD and severe nightmare symptomatology

Aims of this Trial

- Study IR in OEF/OIF/OND Veterans with severe PTSD and recurrent deployment-related nightmares
1. Determine absolute and relative efficacies of two individual cognitive-behavioral treatments in reducing nightmare frequency and distress:
   - cCBT-I: components of CBT for Insomnia
   - cCBT-I plus IR
2. Examine whether treatment effects were modified by baseline variables selected a priori:
   - Gender, race, symptom severity, TBI, and treatment expectancy

Inclusion Criteria

- Male or female Veterans of OEF, OIF or OND
- Current deployment-related PTSD
- Repetitive, military-related nightmares (at least 1 every 2 weeks for at least 6 months)
- A global sleep disturbance (score of 5+ on the PSQI)
- Concurrent anxiety or depressive disorder, alcohol or cannabis abuse diagnoses allowed
- Dementia and amnestic disorder related to head injury allowed
- Concurrent psychiatric and psychotherapy treatment allowed (except concurrent trauma-focused therapy)
  - Medications stable for 2 weeks

Exclusion Criteria

- Substance dependence during the preceding 12 months
- Evidence of "at risk" drinking behavior over the past month
  - More than 4 (women: 3) drinks on a given night, drinking on more than 3 nights a week, or more than 14 total (women: 7) drinks in a week
- Bipolar disorder; delirium; dementia or amnestic disorder not related to head injury; schizophrenia and other psychotic disorder
- Severe TBI
  - Loss of consciousness or alteration of mental status greater than 24 hours, or peri-traumatic memory loss or any posttraumatic amnesia greater than 7 days

Assessment

- Diagnostic assessment with CAPS, SCID
- Self-report baseline and outcome measures including
  - Primary outcomes: Nightmare Frequency Questionnaire (NFQ) and Nightmare Distress Questionnaire (NDQ)
  - Secondary measures: Sleep quality (PSQI), PCL-M, BDI
  - Baseline neuropsychological assessment
- 4 assessment points:
  - Baseline, post-treatment, 3-month follow-up, 6-month follow-up

Interventions: Session by Session

Session	Common Treatment Components (cCBT-I)	IR-specific Treatment Components
1	Psychoeducation, grounding	Intro to IR, rationale
2	PMR	Target dream write-out
3	Sleep hygiene	Brainstorming of possible changes
4	Stimulus control	Rescripting, new dream script write-out
5	Putting the day to rest (cognitive hyperarousal)	Fine-tuning of new script
6	Review, relapse prevention	Fine-tuning of new script

Method

- 2 sites:
  - VA CT Healthcare System in West Haven, CT (n=6)
  - Philadelphia CMCVAMC and its community outpatient clinics (n=102)
- 7 doctoral level psychologists administering the treatment
- Random assignment stratified by site and participant gender
- Treatment fidelity was assessed as *excellent* by a rater independent of the study
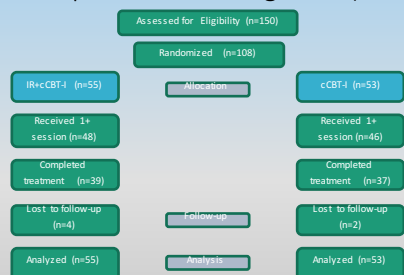
Baseline Characteristics – Demographics

		IR+cCBT-I (N=53)	cCBT-I (N=55)	Total (N=108)
Age	Mean (SD)	37.0 (9.9)	37.2 (10.1)	37.1 (9.9)
Gender	Male	88.7%	83.6%	86.1%
Race	Caucasian	64.2%	52.7%	58.3%
	African American	32.1%	41.8%	37.0%
	Other	3.8%	5.4%	4.6%
Marital Status	Married/Cohabitating	57.7%	44.4%	50.9%
Education	Some college/degree	62.3%	69.1%	65.7%
Employment	Full or part-time	43.4%	43.6%	43.5%
Service Branch	Army	64.2%	61.8%	63.0%
	Navy	3.8%	10.9%	7.4%
	Air Force	11.3%	3.6%	7.4%
	Marines	22.6%	14.6%	18.5%
Deployments	Average Number	2.2	2.2	2.2

Baseline Clinical Characteristics

		IR+cCBT-I (N=53)	cCBT-I (N=55)	Total (N=108)
PTSD symptoms	CAPS severity	87.74 (14.61)	83.27 (14.37)	85.46 (15.62)
	Self-reported: PCL-M	65.75 (9.71)	63.22 (10.36)	64.46 (10.08)
Sleep symptoms	Weekly nights with nightmares (NFQ)	3.71 (1.65)	3.52 (1.75)	3.61 (1.70)
	Weekly number of nightmares (NFQ)	5.76 (4.74)	5.13 (3.74)	5.44 (4.25)
	Nightmare Distress (NDQ)	29.56 (5.91)	29.29 (5.73)	29.43 (5.79)
	Global Sleep Quality (PSQI)	15.85 (2.32)	14.64 (3.17)	15.23 (2.84)*
Comorbidities	Major Depressive Disorder	69.8%	58.2%	63.9%
	Generalized Anxiety Disorder	18.9%	25.4%	22.2%
	Alcohol Abuse	13.2%	1.8%	7.4%*
	Diagnosed TBI	26.4%	38.2%	32.4%
	Self-reported TBI	62.3%	69.1%	65.7%

*p<.05

Participant Flow through Trial (CONSORT)

Assessed for Eligibility (n=150)

Randomized (n=108)

IR+cCBT-I (n=55) — Allocation — cCBT-I (n=53)

Received 1+ session (n=48) — Received 1+ session (n=46)

Completed treatment (n=39) — Completed treatment (n=37)

Lost to follow-up (n=4) — Follow-up — Lost to follow-up (n=2)

Analyzed (n=55) — Analysis — Analyzed (n=53)

Results: Prior and Concurrent Treatments

- 4% had prior course of Prolonged Exposure (of 10-15 sessions); 0% CPT
- 69.4% in concurrent psychotherapy
  - For an average of 8.2 months
- 78.4% were in psychiatric care
  - Average of 11.6 months
- 71% prescribed a psychiatric medication at the time of enrollment
  - Ranging from 1 to 5 medications (mean 1.4).

Results: ITT analyses

- ITT analyses:
  - Longitudinal outcome was analyzed using a mixed effects model with a random intercept for each patient
  - We used the PSQI and CAPS as baseline covariates in the model to control for initial severity
- Main Results:
  - Decreases in nightmare symptoms from baseline to 6 months post treatment for both treatments were <u>statistically significant</u>
  - Intention-to-treat analyses found <u>no differences</u> between therapy groups on primary or secondary outcomes
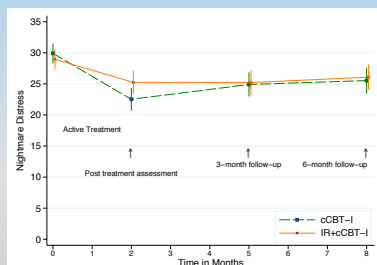
Results: ITT analyses – Nightmare Frequency

- Both treatments showed an average reduction of about one night per week
- Decreasing from 3.6 nights per week to 2.6 nights
- A reduction of almost 30%.

3
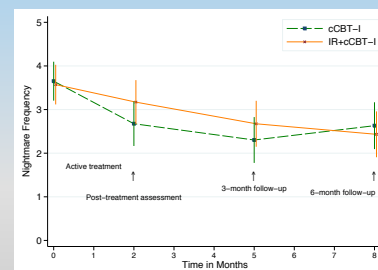
Results: ITT Analyses – Nightmare Distress

- Nightmare distress decreased approximately 4 points
- A reduction of about 14%

Clinically Meaningful Change?

- Clinically important changes in sleep (PSQI drop of 3+ points)
  - 51% with *IR+cCBT-I*
  - 45% with *cCBT-I*
  - Difference not significant ($X^2(2)=0.33, p=0.56$).
- Clinically important decreases in nightmare frequency (decrease of 2+ nightmares/week)
  - *37% with IR+cCBT-I*
  - 32% with *cCBT-I*
  - Difference not significant ($X^2(2)=0.22, p=0.64$)

Treatment Modifying Variables

- Examined variables which may make one of the two treatments more efficacious
  - Gender, race, symptom severity, TBI, and treatment expectancy
  - Did these variables change the relative efficacy of IR+cCBT-I versus cCBT-I?
- No treatment modifying effects for:
  - Race, TBI, expectancy

Treatment Modifiers: Baseline Nightmare Severity
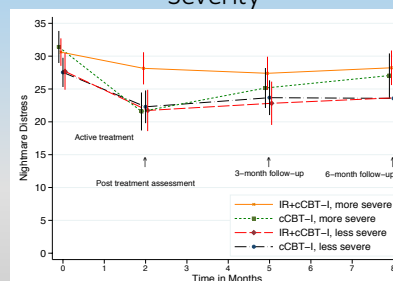
Treatment Modifiers: Gender
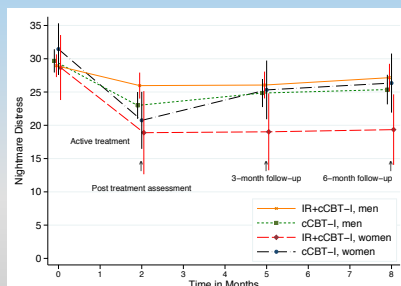
Summary

- Adding IR to cCBT-I did not increase the treatment effect.
- Both treatments succeeded at producing clinically significant decreases in nightmare frequency and sleep disturbance
- Results suggested that IR could improve the treatment gains in specific groups of Veterans:
  - Women
  - Veterans with less severe baseline nightmare disturbance
- Needs replication, but fits with prior research picture

Implications

- As a field we can comfortably say that IR works for some people, but not everyone
- Future directions:
  - Replication!
  - Why may females have a differential treatment response
  - Are there other factors which distinguish those who improved with IR from those who did not?
  - Modifications to IR treatment protocol to increase the potency for those with more severe baseline symptoms

Slide 1

Combat-Related PTSD Nightmares: Which U.S. Veterans Benefit from IR?

Joan M. Cook, Ph.D.
Yale University
National Center for PTSD

Gerlinde Harb, Ph.D.
Richard Ross, M.D., Ph.D.
University of Pennsylvania
Philadelphia CMCVA Medical Center

Andrea Phelps, Ph.D.
Phoenix Australia, University of Melbourne

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Slide 2

ISTSS — International Society for Traumatic Stress Studies — ISTSS 31st Annual Meeting | Back to Basics: Integrating Clinical and Scientific Knowledge to Advance the Field of Trauma | November 5 – 7, 2015, Pre-Meeting Institutes, November 4, New Orleans Marriott, New Orleans, Louisiana, USA — www.istss.org

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Slide 3

Purpose of Presentation

- In order to determine who most benefited from IR, we looked in-depth at data from 29-33 U.S. veterans who <u>completed</u> IR in our RCT:
  - Target nightmare
  - Changed dream script
  - Study therapists' qualitative narratives at end of treatment (e.g., veteran engagement, motivation, and barriers to treatment)
  - Veterans' six-month post-treatment qualitative report on most helpful aspects of therapy

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Slide 4

Nightmare and Dream Script Coding: An Iterative Process

- For our trial in Vietnam War veterans, we devised a nightmare and dream coding system:
  - Reviewed existing tools for rating the phenomenology of nightmares and dreams
  - Developed a new rating tool
- Two licensed clinical psychologists (GH and JC) rated nightmares and dreams independently, and then compared ratings, to arrive at a consensus.

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Slide 5

Example

Nightmare

Changed Dream Script

5

Slide 6

Demographic and Clinical Characteristics

Demographics		Clinical Characteristics: Mean (SD)	
Age	36.2 (10.0)	Weekly number of nightmares (NFQ)	6.0 (4.9)
Gender: Females	9.1%	Weekly number of nights with nightmares (NFQ)	3.7 (1.6)
Race: Non-Caucasian	27.2%	Nightmare distress	28.8 (6.0)
Education: Post HS education	61.6%	PCL-M	63.8 (9.0)
Married/partnered	51.5%	PSQI	15.6 (2.5)
Employed	40.6%	CAPS	84.7 (14.0)
Service connected	69%	BDI	28.0 (11.9)

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Target Nightmares: Pre-Treatment

- Setting: 84% set in deployment
- Degree of trauma replication:
  - 55% replays; 45% mixtures of symbolic and replay
- Life threat: 84% involved life threat
- Gruesome imagery: 68% involved scenes of death
- Primary themes: lack of control or self-efficacy (44%)
- Sensory details: 82% had sensory details
- Emotions: fear (92%), helpless (88%)

7

Dream Scripts: Changes Made

- Most were realistic (66%)
- Most began in a military context and then changed to a different setting (55%)
- Most common themes:
  - Safety (43%)
  - Self-efficacy (27%)
  - Enjoyment-of-life (24%)

8

Relationship of Nightmares and Dream Changes to Outcome

- Pretreatment Nightmare Characteristics:
  - Theme of *guilt* was related to significantly less improvement in *nightmare distress* (r=.48, p<.01).
  - More *life threatening* nightmares were associated with less change in overall *sleep quality* (r=-.53, p<.01).
- Dream Scripts:
  - Types of changes (sensory detail, themes, emotions) made in the dream scripts were generally unrelated to outcome.
    - Only *setting* of new dream script entirely *in deployment* was related to less improvement in *nightmare distress* (r=-.38, p<.05).

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Summary

- Veterans' nightmares were gruesome.
- Guilt nightmares may be more difficult to treat.
- The changes made in the dream scripts were generally not related to outcome.
  - Clinically, we shouldn't suggest one type of change. The changes needs to be "individualized."
  - We may want to encourage our patients to change the setting so that they don't stay in deployment or war-zone scene.
- So what does seem important to promoting improvement?

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Therapist Open-Ended Narratives

- Task: Write narrative after last treatment session:
  - General picture of how therapist viewed the course of change in the patient's nightmare symptoms
  - Patient's level of motivation/compliance
- Coding:
  - What kinds of treatment outcomes were the therapists seeing – what actually changed?
  - What types of changes in nightmares?
  - What factors seemed to contribute to improved outcomes and positive changes in nightmares?

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Changes in Nightmares Based on Therapist Reports

	n	%
No change	3	10
Some change	9	31
Significant change	17	59

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Nature of Changes in Nightmares

	No/Some Change	Significant Change
Nightmare ceased	0 (0%)	6 (35%)*
Dreamed new script content	5 (42%)	8 (48%)
Nightmare shortened	0 (0%)	4 (24%)
Sleeps through nightmare	0 (0%)	6 (35%)*
Added content elements	1 (8%)	5 (29%)
Lucid dreaming**	1 (8%)	4 (24%)

* Significant differences p<.05
** Awareness of ongoing dream and/or active control of dream content

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Types of Nightmare Changes

	No/Some Change	Significant Change
Decreased distress	3 (25%)	12 (71%)*
Decreased frequency	6 (50%)	16 (94%)*
Decreased intensity	2 (17%)	5 (29%)
Other nightmares decreased	0 (0%)	7 (41%)*

* p<.05

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Those with Significant Change

- Timing of changes
  - 17.6% changes in nightmares began after session 2 (nightmare write-out)
  - 29.4% changes in nightmares began after session 3 (brainstorming, suggestions for change)
  - 35.3% changes in nightmares began after session 4 (new script write out)
  - 5.9% changes in nightmares began after session 5 (fine-tuning)
  - 11.8% unclear

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Those With Non-Significant Change

Motivation (ambivalence)

50% Generally not compliant with homework
33% Saw no utility in treatment (low expectancy for change)
33% Not engaged in sessions (passive in participation)
33% Problem with nightmares were not highest priority
25% Skeptical about treatment (rationale or techniques)
25% Found aspect/s of the treatment unacceptable
17% Did not understand rationale
17% Skeptical initially, but eventually accepting

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Level of Engagement

None/Negligible (1)	Attended sessions, but appeared disengaged and completed little or no homework
Low (2)	Attended sessions, appeared engaged but regularly didn't complete homework
Moderate (3)	Attended sessions, engaged, generally completed homework
High (4)	Attended sessions, engaged, always completed homework

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Level of Engagement

- Among those with significant changes:
  - Average = 3.3, sd = .77
- Among those with no/some significant changes:
  - Average = 2.5, sd = .90

- Level of engagement was positively related to whether or not patients had significant changes in their nightmare symptoms ($r = .40$, p=.03)

18

3

Gender Effects?

- Follow-up to RCT findings
- Is there a difference in engagement between men and women?
  - Yes.
    - Men: Mean engagement = 2.88, SD=.86
    - Women: Mean engagement = 4, SD=0
  - Caveat: Only 10% women, i.e., 3 participants

19

Summary

- It seems particularly important that the patient is engaged in IR:
- Retrieval competition hypothesis: If the new imagery is not rehearsed, it is not readily accessible to dreamer and cannot compete with the nightmare images which are well-rehearsed.

20

Patient Self-Report

- Assessment at the final 6-month post-treatment follow-up
- Asked patients what they found helpful in the treatment
- Open-ended questions

21

What Did You find Most Worthwhile And Helpful?

- 81.5% mentioned IR skills
- 70.4% mentioned CBT-I skills

		CBT-I Skills	
IR Skills		No	Yes
	No	0 (0%)	5 (18.5%)
	Yes	8 (29.6%)	14 (51.9%)

- Integration of IR and CBT-I seemed to appeal to participants.

22

Skills Practice at Follow-up

- 92.6% of Veterans told us that they continued to practice skills:
  - On average, they practiced several times a week
  - 33.3% practiced CBT-I skills nightly
  - 11.1 % practiced IR skills nightly
- Level of engagement during treatment was related to continued CBT-I practice (r=.31) and continued IR (r=.24), albeit not statistically significantly
- Those who were rated as having made significant changes in treatment were likely to report applying IR to additional nightmares since treatment (r=.41, p<.05)

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Clinical Implications

- Individualize Treatment:
  - Both ratings of dream scripts and therapist narratives showed that a variety of changes in nightmares can lead to beneficial outcomes.
- Motivation & Engagement in Treatment is Very Important: predicts change during therapy and continued practice
  - Strategies for motivation enhancement may help
  - Likely important to specifically address treatment rationale and barriers to engagement

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Thank you!

Questions, concerns, thoughts,
feel free to email: Joan.Cook@yale.edu

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Slide 1

Effects of Neuropsychological Functioning on Outcomes in a Randomized Trial of Sleep Interventions for PTSD

J. Cobb Scott

Gerlinde C. Harb

Janeese Brownlow

Ruben C. Gur

Richard J. Ross

Philadelphia VAMC & University of Pennsylvania

Slide 2

Acknowledgments

Slide 3

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Slide 4

Purpose of this Presentation

- Towards individualized treatment–which individuals are less (or more) likely to respond to treatment or are at risk for dropping out?
- In order to identify patient characteristics that may impact psychotherapy outcomes, we examined two relevant moderators of treatment outcome in an RCT of Imagery Rehearsal Therapy
  - Traumatic brain injury (mostly mild TBI)
  - Neuropsychological (cognitive) functioning

Slide 5

Background

- PTSD is associated with neuropsychological deficits in attention, executive functions, information processing speed, and episodic learning and memory
- Two meta-analyses in PTSD
  - Brewin et al. (2007) found moderate magnitude effects in verbal memory, and small magnitude effects in nonverbal memory
  - Scott et al. (2015) found moderate magnitude effects in verbal learning and memory, processing speed, attention/working memory, executive functions
    - Treatment-seeking individuals showed even larger cognitive deficits

Slide 6
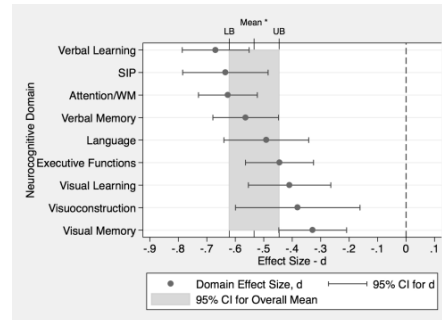
Scott et al., 2015, *Psych Bull*

Background

- Traumatic brain injury (TBI) is prevalent in OEF/OIF Veterans, especially those with PTSD
  - 8%-15% of returning Veterans (Hoge et al., 2008; Vasterling, 2006)
- TBI results in higher severity of mental health, medical, and sleep symptoms (Davis et al., 2013; Towns et al., 2015)
- Still controversy as to whether mild TBI and/or multiple mild TBIs result in *long-term* cognitive dysfunction (Bigler et al., 2013; Boyle et al., 2014)
  - Dysfunction in prefrontal brain networks, which can disrupt a variety of executive functions and memory encoding
- Perception that Veterans with TBI may not fully benefit from psychotherapy because of cognitive limitations, impulsivity, and emotional dysregulation (Wolf et al., 2015)

Significance

- Psychotherapy (especially CBT) relies heavily on neurocognitive skills to achieve treatment gains, including
  - Verbal abilities (e.g., discussing trauma narratives)
  - Verbal memory (e.g., remembering treatment discussions, consolidating)
  - Executive functions (e.g., self-monitoring, working memory, sustained attention)

Significance

- Neuropsychological functioning rarely explored as influential factor in psychotherapy treatment
  - Robust association with treatment compliance and outcomes in substance use treatment (Aharonovich, Nunes, & Hasin, 2003)
- Wild and Gur (2008) – treatment non-responders showed worse immediate verbal memory at baseline, and change in PTSD symptoms was associated with verbal memory
- Nidjam et al. (2015) – pre-treatment verbal memory functioning was associated with degree of change in PTSD symptoms across two kinds of trauma-focused therapies

Methods

- Veteran participants in RCT of Imagery Rehearsal (IR) for recurrent, PTSD-related nightmares
- At baseline, 94 (out of 108) received neuropsychological testing via Penn Computerized Neurocognitive Battery (CNB) (Gur et al., 2001, 2010, 2012)
  - Widely validated battery of tests assessing attention, executive functioning, learning and memory, and visuospatial processing
  - Analyses focused on verbal list learning and n-back working memory measure
- Also detailed assessment of TBI history

Aims

- Aim 1: Determine whether Veterans with PTSD+TBI show equivalent treatment benefit to those with PTSD only
  - H1: TBI would not moderate treatment response but would show main effects (i.e., be more symptomatic at all timepoints)
- Aim 2: Examine the influence of neuropsychological functioning on treatment outcomes
  - H1: Verbal immediate memory and working memory would moderate treatment response across both treatments

Statistical Analyses

- Mixed-effects, repeated-measures analyses with a random intercept for each patient
  - Separate models analyzed outcomes as a function of TBI*time and cognitive performance*time, as well as main effects
  - Each model included treatment*time interaction term
  - Follow-up analyses included covariates for depression and overall cognitive performance to examine specificity of effects
- Analyses focused on: 1) nightmare distress (NDQ); 2) total sleep disturbance (PSQI); 3) total nightmare nights per week (NFQ)
- Logistic regression analyses to examine dropout (< 5/6 visits)

Participant Characteristics

	Subsample (n= 94)	Total Sample (n= 108)
	Mean (SD)	Mean (SD)
Age	37.1 (9.9)	37.1 (9.9)
Education (some college/degree)	64.1%	65.7%
% Male	85.3%	86.1%
Caucasian (%)	59.0%	58.3%
African-American (%)	35.8%	37.0%
Other (%)	5.3%	4.6%
TBI (%)	66.3%	65.7%
TBI with Loss of Consciousness (%)	34.7%	36.5%
Nightmare Distress (NDQ)	29.4 (5.92)	29.43 (5.79)
Global Sleep Quality (PSQI)	15.38 (2.77)	15.23 (2.84)
Weekly nights with nightmares (NFQ)	3.69 (1.68)	3.61 (1.70)
Weekly number of nightmares (NFQ)	5.49 (4.18)	5.44 (4.25)

Results
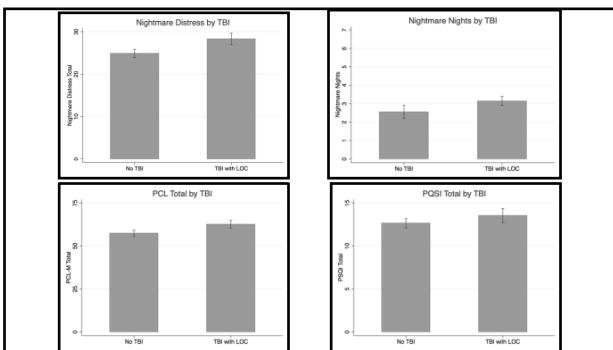
TBI Results

- Main effect of TBI on nightmare distress (*p*=0.004) and nightmare nights (*p*=0.015)
- General pattern—start and stay more symptomatic
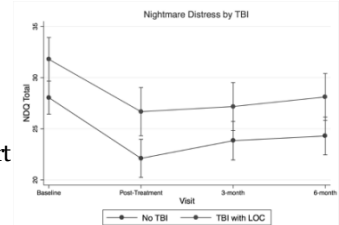
Verbal Memory Results

- Significant verbal memory*time interaction for nightmare distress (*p* = .0005)
- Still significant (*p* < .01) after including depression and overall neurocognitive performance as covariates in model
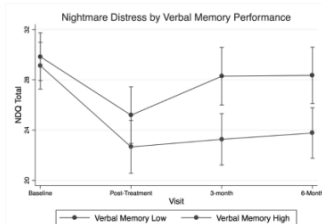
Verbal Memory Results

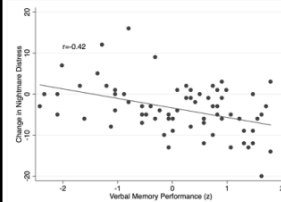- Verbal memory*time interaction not significant for number of nightmare nights (*p* = 0.40)
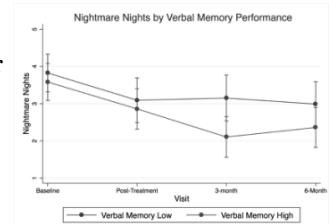
Verbal Memory Results

- Significant verbal memory*time interaction for PSQI ($p = 0.02$)
- Still significant after including overall cognitive performance as covariate in model, but including depression reduced interaction to trend ($p=0.07$)
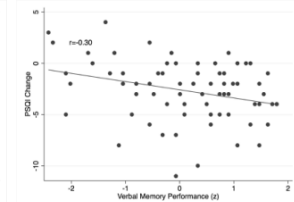

PSQI Total by Verbal Memory Performance
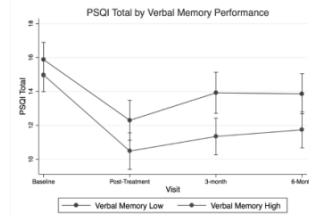
Results

Change in Nightmare Distress   Change in PSQI

Working Memory Results

- No significant working memory*time interactions or main effects of working memory performance on outcomes ($ps > .10$)

Dropout Results

- Individuals with TBI not significantly more likely to drop out of treatment (OR = 0.97; p=.88)
- Neither verbal memory (OR = 0.93; p=.73) nor working memory performance (OR = 0.64; p=.06) associated with treatment dropout

---

Discussion

- Verbal memory performance moderated treatment outcomes across two types of short-term psychotherapy sleep interventions
  - Individuals with lower performance less likely to respond to treatment
- In combination with prior findings, results suggest that verbal memory may be important factor to consider to optimize psychotherapy treatment outcomes in PTSD
  - Also, specificity of verbal memory

Discussion

- TBI may be important to consider in terms of symptom severity but did not moderate treatment response
- Neither TBI nor cognitive performance was associated with treatment dropout

Future Directions

- Further research on the *pathways* by which neurocognitive functioning may affect treatment outcomes
  - Direct interference with treatment comprehension and implementation (i.e., one's ability to benefit from the primary "active ingredient" of treatment)?
  - Treatment engagement?
- "Fine tuned" treatments, presented at the appropriate cognitive level and format, may be critical for treatment effectiveness
  - Repetition, reduced memory demands
- Need development and further study

Thank you!

Extra Slides

Results

- Significant main effect of TBI on Significant TBI*time interaction on nightmare nights
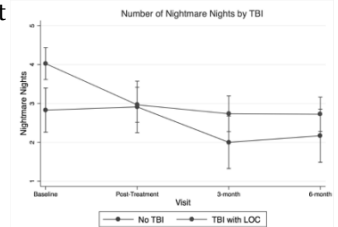
Treatment Seeking Status

- Individuals seeking treatment for PTSD had larger neurocognitive effects in prior meta-analysis
- Clinically, may mean that those with PTSD presenting for treatment need more attention to cognition in order to optimize treatment outcomes
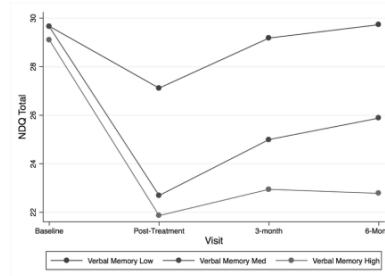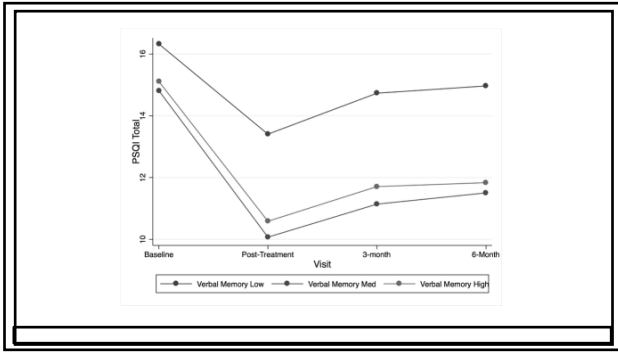
Treating Posttraumatic Sleep Disturbance in U.S. Veterans Who Served in Iraq and Afghanistan: Findings from a Randomized Controlled Trial

Richard J. Ross, M.D., Ph.D.

Michael J. Crescenz VA Medical Center

Perelman School of Medicine

University of Pennsylvania

Supported by the U.S. Department of Defense
CDMRP Award Number W81XWH-08-20104

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I, Richard Ross, have no commercial relationships to disclose. Prazosin is not FDA-approved for the treatment of recurrent nightmares.

Nightmare Disturbance in PTSD

- Trauma-related anxiety dreams are the problem reported most consistently by Veterans with PTSD (Neylan et al. 1998).
- These dreams can persist for more than 40 years after a traumatic event (Neylan et al. 1998).

Nightmare Disturbance in PTSD

- In a RCT of CPT and PE for female rape victims with PTSD, sleep disturbance (including nightmare severity) did not remit (Gutner et al. 2013).
- Antidepressant medications may exacerbate the sleep disturbance.
- RCTs of prazosin have shown promise (Raskind et al. 2003, 2007, 2008, 2013).
- Imagery rehearsal has shown promise, but there are conflicting findings.

Difficulty in treating posttraumatic nightmares: Insights from neurobiology

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Pathophysiology of Nightmares

- Most nightmares emerge from REM sleep
- In PET studies in humans, deactivation of vast areas of dorsolateral prefrontal cortex during REM sleep has been identified (Maquet et al. 1996).
- "The inactivity of lateral PFC and parietal regions during REM has been widely speculated to underlie executive deficits in dreaming…" (Pace-Schott 2011)
- It may be difficult to effect top-down control of nightmare content and generation.

Mechanism of Imagery Rehearsal

- Yet it is such a top-down control of nightmare content and generation that IR requires.
- How does dream rescripting during waking, as in IR, influence REM sleep and REM dreams?
  - it is of some help to know that REM sleep is characterized by a desynchronized EEG like that of waking

REM Sleep Promoting Cognitive-behavioral Change

- It also is of help to know that REM sleep is malleable, influenced by waking experience.
- " … temporally sequenced ensemble firing rate patterns reflecting … behavioral experience [during waking] are reproduced during REM episodes at an equivalent time scale." (Louie and Wilson 2001)

REM Sleep Promoting Emotional Change

- There is other evidence that REM sleep is malleable, and in fact plays a central role in the processing of emotion.
- Normal dreaming may promote the consolidation of fear extinction memories; it is a dysfunction of the responsible affective network that leads to dysphoric dreaming, including nightmares (Levin and Nielsen 2007).

Predictors of Responsiveness to IR

Nightmare Themes

- The theme of *guilt* was related to significantly less improvement in nightmare distress ($r = -.48$, $p<.01$).
- Only in 2005 did the ICSD-2 acknowledge that nightmares could involve dysphoric emotions other than fear and anxiety (Levin and Nielsen 2007).
- Increasing evidence suggests that many Veterans are most troubled by experiences in war not adequately characterized as life threatening (Stein et al. 2012).
- How is moral injury different from a life threat stressor?
  - Compared to a life threat stressor, does moral injury affect nightmare construction and themes differently?
  - How should stressor type and nightmare type influence the choice of IR as a nightmare treatment?

Gender and Nightmares

- The current trial suggests that women may show greater responsiveness to IR.
- Women report more nightmares than men.
- " … biological differences in emotional brain processes may be responsible" (Levin and Nielsen 2007)
- Such differences may enter into a differential responsiveness of women to treatment with IR.
- The existing IR literature may be confounded by gender effects.
- Future nightmare research must consider the influence of gender on treatment response.

Gender and Engagement

- Level of engagement was positively related to whether or not participants had significant changes in nightmare symptoms.
- Women showed greater engagement than men (small N)
- " ... not only do women have higher rates of dream recall than men, but they rate both their dreams and nightmares as more vivid and *meaningful* ... and report that their dreams have *greater impact* on their waking behavior than do men." (reviewed in Levin and Nielsen 2007)
- Does the influence of gender on responsiveness to IR depend on engagement?

Engagement

- Engagement may require treatment-matching, but treatment-matching requires knowledge.
- There are limited meaningful data with which to educate patients about treatment approaches that may be especially helpful to them personally (Kearney and Simpson 2015).
- A pilot study in OEF/OIF Veterans showed that a brief shared decision-making intervention could enhance engagement in evidence-based PTSD treatment (Mott et al. 2014).
- Personalized treatment for posttraumatic nightmares will depend on both research identifying predictors and clinical procedures for sharing decision-making.

PTSD Severity

- The current trial suggests that individuals with less severe PTSD may show greater responsiveness to IR.
- In a recent meta-analysis of psychotherapy treatment studies in Veterans and active duty military personnel, both low and high PTSD severity levels, compared with a moderate severity level, were associated with poor outcome (Haagen et al. 2015).
- Haagen et al. (2015) emphasized the importance of titrating the level of emotional activation as evidence-based therapy proceeds.
- IR has an exposure component, and a similar titration strategy may be required.

Neuropsychological Functioning

- The current trial suggests that verbal memory abilities may moderate treatment response.
- The dorsolateral prefrontal cortex may be taken off-line by heightened release of catecholamines (Arnsten 2015).
- There is substantial evidence for noradrenergic hyperactivity in PTSD (Southwick et al. 1999).
- There is evidence from RCTs that the alpha-1 adrenoceptor antagonist prazosin ameliorates the nightmare disturbance in PTSD (Raskind 2009).
- Would concurrent prazosin treatment add to the efficacy of IR?
- Would prazosin be the preferred treatment in individuals with seriously impaired neuropsychological functioning?
- Should neuropsychological testing be included in the initial assessment of patients for nightmare therapy?

Conclusions

- Recurrent posttraumatic nightmares are prevalent, cause great functional impairment, and are difficult to treat.
- Continuing research into the pathophysiology of nightmares is essential.
- Personalized treatment will depend on identifying factors that moderate treatment response.
- These factors may include: nightmare theme, stressor type, gender, engagement in treatment, PTSD severity, and neuropsychological functioning.